# Synthesis of 4-benzylpyridines via Pd-catalyzed $CH_3$-arylation of 4-picoline

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## Supporting Information

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## 1. General information

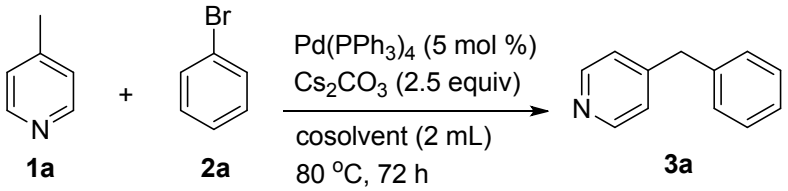
$^{1}H$ NMR, $^{13}C$ NMR and $^{19}F$ NMR were recorded in $CDCl_3$ at room temperature on the Bruker AVⅢ-400 spectrometer (400 MHz, $^{1}H$). The chemical-shifts scale is based on internal TMS. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; qui, quintet; sxt, sextet. The coupling constants, J are reported in Hertz (Hz). High-resolution mass spectral (HRMS) analyses were carried out using a TOF MS instrument with an ESI source.

Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification, all reactions were run under $N_2$ and were heated in the oil bath, Fresh catalyst $Pd(PPh_3)_4$ were used in all experiments. Prior to starting experiments, the reaction flask must be heated by using heat gun in vacuum, then the base $Cs_2CO_3$ must be heated by using heat gun as well. Products were purified by flash column chromatography on 200-300 mesh silica gel, $SiO_2$.

## 2. Pd-catalyzed arylation of 4-methylpyridine

### 2.1 Optimization of reaction conditions

**Table 1. Screening of reaction solvents**[a]

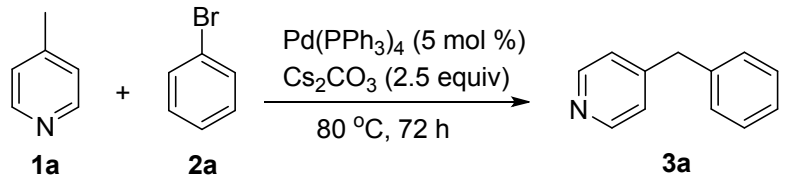



**1a** **2a** **3a**

| entry | cosolvent | Yield (%)[b] |
|---|---|---|
| 1 | 4-picoline[c] | 86 |
| 2 | DMF | 14 |
| 3 | DMSO | 6 |
| 4 | Dioxane | 0 |
| 5 | DMI | 0 |
| 6 | NMP | 0 |
| 7 | toluene | 10 |
| 8 | THF | 0 |

[a]Reaction conditions: **1a** (5.0 mmol), **2a** (0.5 mmol), $Pd(PPh_3)_4$ (0.025 mmol), $Cs_2CO_3$ (1.25 mmol), cosolvent (2.0 mL), under 80 °C, 72 h. [b]Isolated yields. [c]Reaction conditions: **1a** (3.0 mL), **2a** (0.5 mmol), $Pd(PPh_3)_4$ (0.025 mmol), $Cs_2CO_3$ (1.25 mmol), under 80 °C, 72 h.

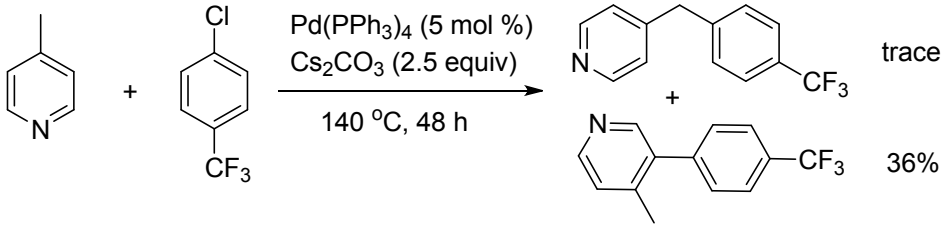
**2.2 General procedure for Pd-catalyzed arylation of 4-methylpyridine**




**1a** **2a** **3a**

To a dried 25 mL sealed tube, were added the base $Cs_2CO_3$ (407 mg, 1.25 mmol), then it must be heated by using heat gun in vacuum. And **2a** (78.5 mg, 0.5 mmol), **1a** (3 mL), $Pd(PPh_3)_4$ (29 mg, 0.025 mol) were added in the tube when it changed room temperature. The tube was capped and stirred at 80 °C for 72 h. The reaction mixture was cooled to room temperature and quenched with water. It was extracted 3 times by using EtOAc, the organic phase was combined and dried with $Mg_2SO_4$, then concentrated. The resulting residue was purified by chromatography on silica gel (petroleum ether/triethylamine = 20: 1) to give the pure compound **3a**.

**2.3 Reaction of coupling 4-picoline with 1-chloro-4-(trifluoromethyl)benzene**

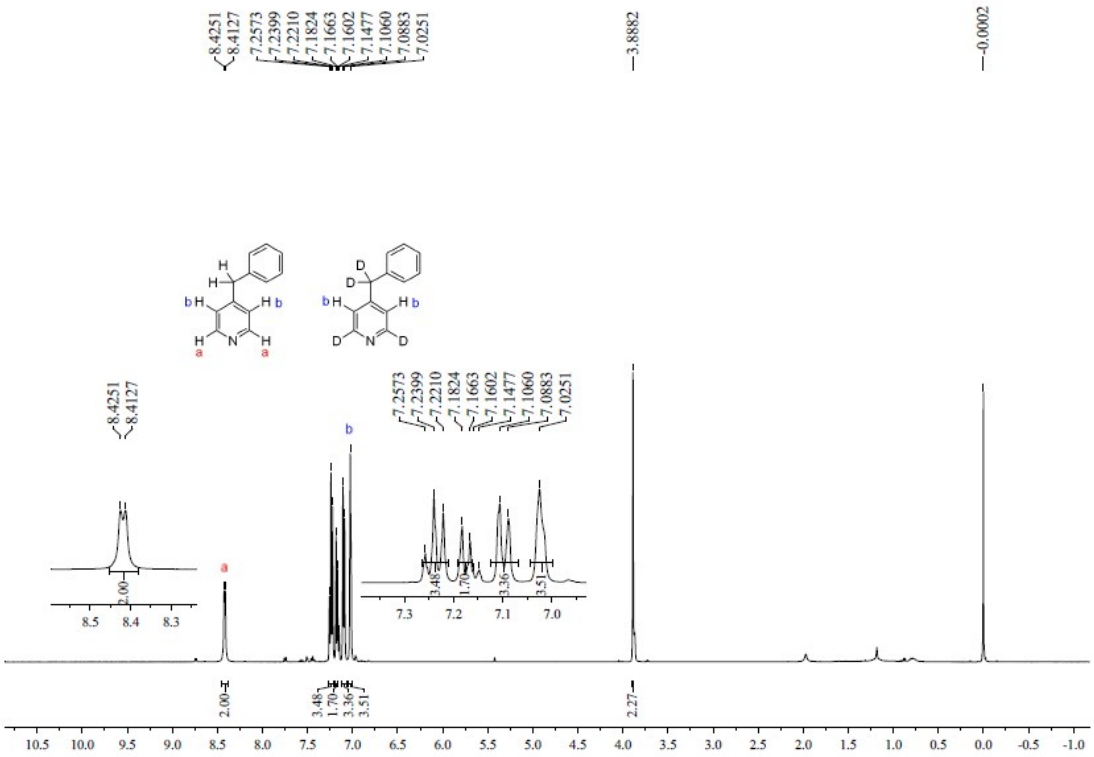



To a dried 25 mL sealed tube, were added the base $Cs_2CO_3$ (407 mg, 1.25 mmol), then it must be heated by using heat gun in vacuum. And 1-chloro-4-(trifluoromethyl)benzene (90 mg, 0.5 mmol), 4-picoline (3 mL), $Pd(PPh_3)_4$ (29 mg, 0.025 mol) were added in the tube when it changed room temperature. The tube was capped and stirred at 140 °C for 48 h. The reaction mixture was cooled to room temperature and quenched with water. Then it was extracted 3 times by using EtOAc, the organic phase was combined and dried with $Mg_2SO_4$, then concentrated. The resulting residue was purified by chromatography on silica gel (petroleum ether/triethylamine = 20: 1) to give the pure compound 4-methyl-3-(4-(trifluoromethyl)phenyl)pyridine. 4-methyl-3-(4-(trifluoromethyl)phenyl)pyridine[1]: 42 mg, 36% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.41 (d, $J$ = 5.0 Hz, 1H), 8.35 (s, 1H), 7.64 (d, $J$ = 8.0 Hz, 2H), 7.37 (d, $J$ = 8.0 Hz, 2H), 7.14 (d, $J$ = 5.0 Hz, 1H).

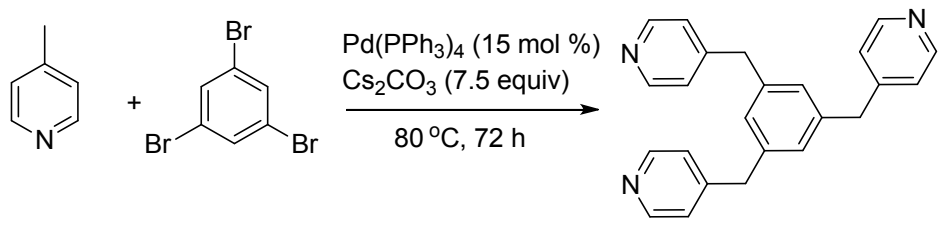
**2.4 Control experiments**

To two dried 25 mL sealed tubes, were added respectively the base $Cs_2CO_3$ (407 mg, 1.25 mmol),

then they must be heated by using heat gun in vacuum. After cooling down to rt, bromobenzene (78.5 mg, 0.5 mmol), **1a** (1.5 mL, 15.4 mmol) or **1a-*d*$_5$** (1.5 mL, 15.4 mmol), $Pd(PPh_3)_4$ (29 mg, 0.025 mol) were added in the tubes. The tubes were capped and stirred at 80 $^oC$ for 72 h. The two reaction mixtures were cooled to room temperature, combined and quenched with water. The mixture was extracted 3 times by using EtOAc, the organic phase was combined and dried with $Mg_2SO_4$, then concentrated. The resulting residue was purified by chromatography on silica gel (petroleum ether/triethylamine = 20:1) to give the product **3a** and **3a-*d*$_4$** in less than 50% yield. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.41 (d, $J$ = 5.0 Hz, 2H), 7.24 (t, $J$ = 7.0 Hz, 3.47H), 7.17 (d, $J$ = 6.4 Hz, 1.74H), 7.10 (d, $J$ = 7.1 Hz, 3.30H), 7.03 (s, 3.47H), 3.89 (s, 2.29H). The KIE value was calculated as $k_H/k_D$ = 1.45.




**2.5 Synthesis of 1,3,5-tris(pyridin-4-ylmethyl)benzene**

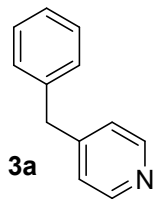



To a dried 25 mL sealed tube, were added the base $Cs_2CO_3$ (1.222g, 3.75 mmol), then it must be heated by using heat gun in vacuum. And 1,3,5-tribromobenzene (155.5mg, 0.5 mmol), 4-pycoline

(3 mL), $Pd(PPh_3)_4$ (87 mg, 0.075 mmol) were added in the tube when it changed room temperature. The tube was capped and stirred at 80 °C for 72 h. The reaction mixture was cooled to room temperature, and was extracted 3 times by using EtOAc, the organic phase was combined and dried with $Mg_2SO_4$, then concentrated. The resulting residue was purified by chromatography on silica gel (petroleum ether/triethylamine = 15: 1) to give the desired product. 1,3,5-tris(pyridin-4-ylmethyl)benzene Synthesis[2]: 70 mg, 40% yield, white solid, mp: 102–106 °C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.42 (d, $J$ = 5.8 Hz, 6H), 6.98 (d, $J$ = 5.7 Hz, 6H), 6.79 (s, 3H), 3.83 (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 148.91, 148.54, 138.93, 127.11, 123.07, 39.97; HRMS (ESI) calcd for $C_{24}H_{21}N_3$ $(M + H)^+$ 352.1815, found 352.1806.

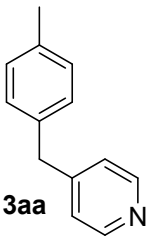
**3. Characterization data of products**

**4-benzylpyridine (3a)**[3]



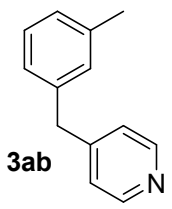

*Compound* ***3a***: 72 mg, 86% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.42 (d, $J$ = 6.0 Hz, 2H), 7.23 (t, $J$ = 7.5 Hz, 2H), 7.17 (d, $J$ = 6.7 Hz, 1H), 7.09 (d, $J$ = 7.2 Hz, 2H), 7.02 (d, $J$ = 5.8 Hz, 2H), 3.88 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 148.95, 148.81, 137.85, 128.01, 127.70, 125.65, 123.14, 40.21.

**4-(4-methylbenzyl)pyridine (3aa)**[4]



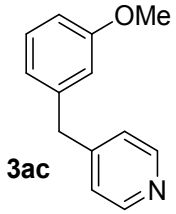

*Compound* ***3aa***: 67 mg, 74% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.48 (d, $J$ = 5.8 Hz, 2H), 7.09 (m, 6H), 3.92 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 149.29, 148.78, 135.23, 134.79, 128.37, 127.88, 123.11, 39.79, 20.00; HRMS (ESI) calcd for $C_{13}H_{13}N$ $(M + H)^+$ 184.1128, found 184.1117.

**4-(3-methylbenzyl)pyridine (3ab)**[5]




*Compound* ***3ab***: 67 mg, 74% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.39 (d, $J$ = 5.9 Hz, 2H), 7.10 (t, $J$ = 7.5 Hz, 1H), 6.99 (d, $J$ = 5.7 Hz, 2H), 6.95 (d, $J$ = 7.5 Hz, 1H), 6.87 (d, $J$ = 8.2 Hz, 2H), 3.81 (s, 2H), 2.22 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 149.07, 148.78, 137.75, 137.31, 128.75, 127.56, 126.36, 125.02, 123.13, 40.13, 20.32; HRMS (ESI) calcd for $C_{13}H_{13}N$ $(M + H)^+$ 184.1128, found 184.1128.

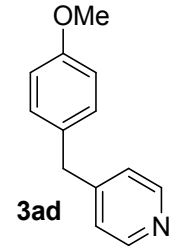
**4-(3-methoxybenzyl)pyridine (3ac)**[6]



**3ac**

*Compound **3ac***: 69 mg, 70% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.40 (d, $J$ = 5.9 Hz, 2H), 7.14 (t, $J$ = 8.0 Hz, 1H), 7.01 (d, $J$ = 5.7 Hz, 2H), 6.69 (t, $J$ = 7.5 Hz, 2H), 6.62 (s, 1H), 3.84 (s, 2H), 3.68 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 158.84, 148.82, 148.78, 139.36, 128.68, 123.12, 120.38, 113.93, 110.78, 54.13, 40.19; HRMS (ESI) calcd for $C_{13}H_{13}NO$ $(M + H)^+$ 200.1077, found 200.1073.

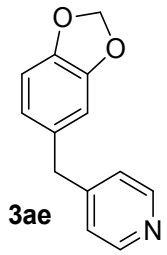
**4-(4-methoxybenzyl)pyridine (3ad)**[5]



**3ad**

*Compound **3ad***: 66 mg, 67% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.41 (d, $J$ = 5.7 Hz, 2H), 7.02 (m, 4H), 6.78 (d, $J$ = 8.6 Hz, 2H), 3.83 (s, 2H), 3.72 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 157.38, 149.45, 148.82, 129.92, 123.05, 113.12, 54.26, 39.34; HRMS (ESI) calcd for $C_{13}H_{13}NO$ $(M + H)^+$ 200.1077, found 200.1078.

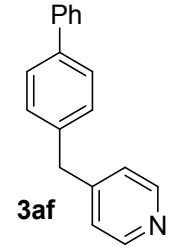
**4-(benzo[d][1,3]dioxol-5-ylmethyl)pyridine (3ae)**[5]



**3ae**

*Compound **3ae***: 76 mg, 72% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.42 (d, $J$ = 5.8 Hz, 2H), 7.02 (d, $J$ = 5.5 Hz, 2H), 6.69 (d, $J$ = 7.7 Hz, 1H), 6.57 (d, $J$ = 8.8 Hz, 2H), 5.86 (s, 2H), 3.80 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 149.12, 148.85, 146.92, 145.33, 131.57, 123.00, 121.00, 108.39, 107.37, 99.99, 39.88; HRMS (ESI) calcd for $C_{13}H_{11}NO_2$ $(M + H)^+$ 214.0870, found 214.0869.

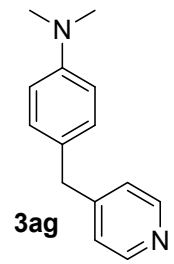
**4-([1,1'-biphenyl]-4-ylmethyl)pyridine (3af)**



**3af**

*Compound **3af***: 87 mg, 71% yield, white solid, mp: 68–70 $^o$C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.43 (d, $J$ = 5.8 Hz, 2H), 7.47 (m, 4H), 7.34 (t, $J$ = 7.8 Hz, 2H), 7.25 (d, $J$ = 7.4 Hz, 1H), 7.15 (d, $J$ = 8.0 Hz, 2H), 7.05 (d, $J$ = 5.6 Hz, 2H), 3.90 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 148.88, 148.85, 139.67, 138.64, 136.90, 128.41, 127.75, 126.41, 126.25, 125.98, 123.16, 39.84; HRMS (ESI) calcd for $C_{18}H_{15}N$ $(M + H)^+$ 246.1284, found 246.1278

**N,N-dimethyl-4-(pyridin-4-ylmethyl)aniline (3ag)**[5]

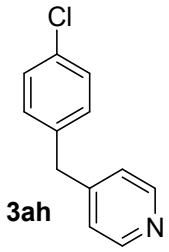


**3ag**

*Compound **3ag***: 18 mg, 17% yield, white solid, mp: 42–43 $^o$C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.40 (d, $J$ = 5.8 Hz, 2H), 7.02 (d, $J$ = 5.6 Hz, 2H), 6.96 (d, $J$ = 8.6 Hz, 2H), 6.62 (d, $J$ = 8.6 Hz, 2H), 3.79 (s, 2H), 2.85 (s, 6H); $^{13}$C NMR

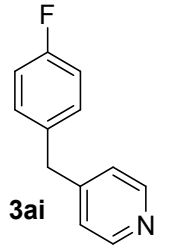
(100 MHz, $CDCl_3$): $\delta$ 150.04, 148.70, 148.44, 128.66, 125.70, 123.07, 111.88, 39.55, 39.26; HRMS (ESI) calcd for $C_{14}H_{16}N_2$ $(M + H)^+$ 213.1393, found 213.1392.

**4-(4-chlorobenzyl)pyridine (3ah)**[7]



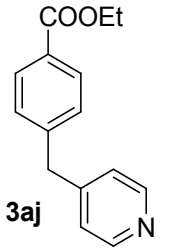

*Compound **3ah***: 75 mg, 75% yield, colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.42 (dd, $J$ = 6.0, 3.0 Hz, 2H), 7.19 (m, 2H), 7.00 (m, 4H), 3.84 (s, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 148.94, 148.33, 136.29, 131.54, 129.33, 127.82, 123.03, 39.47; HRMS (ESI) calcd for $C_{12}H_{10}ClN$ $(M + H)^+$ 204.0582, found 204.0581.

**4-(4-fluorobenzyl)pyridine (3ai)**[8]



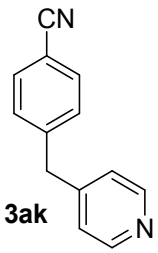

*Compound **3ai***: 71 mg, 76% yield, colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.42 (d, $J$ = 5.9 Hz, 2H), 7.05 (m, 2H), 7.00 (d, $J$ = 5.7 Hz, 2H), 6.92 (t, $J$ = 8.6 Hz, 2H), 3.86 (s, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 148.93, 148.74, 133.52 (d, $J$ = 3.4 Hz), 129.46 (d, $J$ = 10.2 Hz), 123.02, 114.65, 114.44, 39.35; $^{19}F$ NMR (375 MHz, $CDCl_3$): $\delta$ -116.24; HRMS (ESI) calcd for $C_{12}H_{10}FN$ $(M + H)^+$ 188.0877, found 188.0874.

**ethyl 4-(pyridin-4-ylmethyl)benzoate (3aj)**[5]



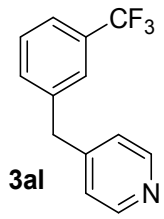

*Compound **3aj***: 80 mg, 67% yield, colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.43 (d, $J$ = 5.9 Hz, 2H), 7.91 (d, $J$ = 8.2 Hz, 2H), 7.16 (d, $J$ = 8.0 Hz, 2H), 7.00 (d, $J$ = 5.9 Hz, 2H), 4.29 (q, $J$ = 7.1 Hz, 2H), 3.93 (s, 2H), 1.30 (t, $J$ = 7.1 Hz, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 165.30, 148.98, 147.98, 142.97, 128.98, 128.05, 128.00, 123.10, 59.91, 40.11, 13.30; HRMS (ESI) calcd for $C_{15}H_{15}NO_2$ $(M + H)^+$ 242.1183, found 242.1179.

**4-(pyridin-4-ylmethyl)benzonitrile (3ak)**[5]




*Compound **3ak***: 73 mg, 76% yield, colorless oil; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.45 (d, $J$ = 5.8 Hz, 2H), 7.53 (d, $J$ = 8.2 Hz, 2H), 7.21 (d, $J$ = 8.0 Hz, 2H), 7.01 (d, $J$ = 5.6 Hz, 2H), 3.95 (s, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 149.16, 147.12, 143.35, 131.53, 128.77, 123.09, 117.64, 109.79, 40.17; HRMS (ESI) calcd for $C_{13}H_{10}N_2$ $(M + H)^+$ 195.0924, found 195.0918.

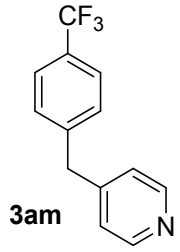
**4-(3-(trifluoromethyl)benzyl)pyridine (3al)**[5]



3al

*Compound* ***3al***: 104 mg, 88% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.44 (d, $J$ = 5.8 Hz, 2H), 7.43 (d, $J$ = 7.6 Hz, 2H), 7.36 (m, 2H), 7.26 (d, $J$ = 7.6 Hz, 1H), 7.01 (d, $J$ = 5.6 Hz, 2H), 3.93 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 149.06, 147.81, 138.78, 131.39, 130.09 (q, $J$ = 32.1 Hz), 128.20, 124.68 (q, $J$ = 3.76 Hz), 123.06, 123.01 (d, $J$ = 270.73 Hz), 122.63 (q, $J$ = 3.73 Hz), 39.90; $^{19}$F NMR (375 MHz, $CDCl_3$): $\delta$ -62.63; HRMS (ESI) calcd for $C_{13}H_{10}F_3N$ $(M + H)^+$ 238.0845, found 238.0847.

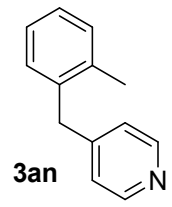
**4-(4-(trifluoromethyl)benzyl)pyridine (3am)**



3am

*Compound* ***3am***: 97 mg, 82% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.45 (d, $J$ = 5.9 Hz, 2H), 7.49 (d, $J$ = 8.0 Hz, 2H), 7.21 (d, $J$ = 8.0 Hz, 2H), 7.01 (d, $J$ = 5.7 Hz, 2H), 3.94 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 149.07, 147.75, 141.91, 128.34, 128.30 (d, $J$ = 65.9 Hz), 126.67 (q, $J$ = 3.77 Hz), 123.12 (d, $J$ = 270.2 Hz), 123.09, 39.94; $^{19}$F NMR (375 MHz, $CDCl_3$): $\delta$ -62.48; HRMS (ESI) calcd for $C_{13}H_{10}F_3N$ $(M + H)^+$ 238.0845, found 238.0847.

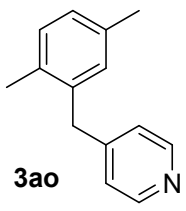
**4-(2-methylbenzyl)pyridine (3an)**[7]



3an

*Compound* ***3an***: 32 mg, 35% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.40 (dd, $J$ = 6.0, 3.0 Hz, 2H), 7.11 (m, 3H), 7.04 (m, 1H), 6.97 (d, $J$ = 6.0 Hz, 2H), 3.91 (s, 2H), 2.13 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 148.76, 148.54, 135.73, 135.62, 129.53, 129.09, 126.08, 125.23, 122.95, 37.85, 18.57; HRMS (ESI) calcd for $C_{13}H_{13}N$ $(M + H)^+$ 184.1128, found 184.1121.

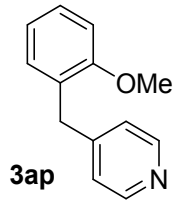
**4-(2,5-dimethylbenzyl)pyridine (3ao)**



3ao

*Compound* ***3ao***: 41 mg, 43% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.40 (d, $J$ = 5.8 Hz, 2H), 7.00 (d, $J$ = 7.6 Hz, 1H), 6.97 (d, $J$ = 5.5 Hz, 2H), 6.93 (d, $J$ = 8.0 Hz, 1H), 6.85 (s, 1H), 3.86 (s, 2H), 2.23 (s, 3H), 2.08 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 148.77, 148.68, 135.53, 134.69, 132.40, 129.86, 129.43, 126.71, 122.96, 37.83, 19.90, 19.08; HRMS (ESI) calcd for $C_{14}H_{15}N$ $(M + H)^+$ 198.1284, found 198.1270.

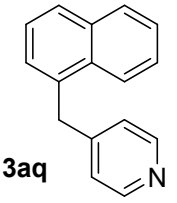
**4-(2-methoxybenzyl)pyridine (3ap)**



3ap

*Compound **3ap***: 49 mg, 50% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.38 (d, $J$ = 5.9 Hz, 2H), 7.16 (m, 1H), 7.03 (d, $J$ = 5.9 Hz, 3H), 6.83 (m, 2H), 3.88 (s, 2H), 3.71 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 156.34, 149.18, 148.58, 129.49, 127.13, 126.42, 123.11, 119.59, 109.56, 54.27, 34.57; HRMS (ESI) calcd for $C_{13}H_{13}NO$ $(M + H)^+$ 200.1077, found 200.1071.

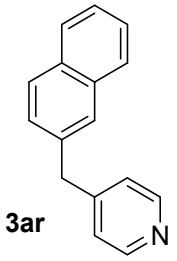
**4-(naphthalen-1-ylmethyl)pyridine (3aq)**[9]



3aq

*Compound **3aq***: 70 mg, 64% yield, white solid, mp: 81–82 $^o$C; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.37 (d, $J$ = 5.8 Hz, 2H), 7.75 (m, 3H), 7.35 (m, 3H), 7.22 (d, $J$ = 6.9 Hz, 1H), 6.98 (d, $J$ = 5.4 Hz, 2H), 4.31 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 148.83, 148.66, 133.38, 132.97, 130.85, 127.80, 126.77, 126.67, 125.23, 124.77, 124.50, 122.90, 122.88, 37.43; HRMS (ESI) calcd for $C_{16}H_{13}N$ $(M + H)^+$ 220.1128, found 220.1108.

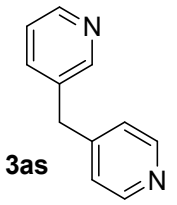
**4-(naphthalen-2-ylmethyl)pyridine (3ar)**[9]



3ar

*Compound **3ar***: 71 mg, 65% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.41 (dd, $J$ = 6.0, 2.9 Hz, 2H), 7.70 (m, 3H), 7.53 (s, 1H), 7.34 (m, 2H), 7.17 (dd, $J$ = 1.7, 1.8Hz, 1H), 7.03 (d, $J$ = 6.0 Hz, 2H), 4.01 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 148.87, 148.78, 135.28, 132.50, 131.20, 127.40, 126.64, 126.51, 126.44, 126.28, 125.23, 124.70, 123.21, 40.31; HRMS (ESI) calcd for $C_{16}H_{13}N$ $(M + H)^+$ 220.1128, found 220.1124.

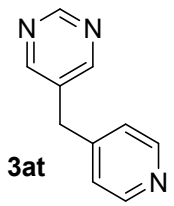
**3-(pyridin-4-ylmethyl)pyridine (3as)**



3as

*Compound **3as***: 60 mg, 71% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.44 (m, 4H), 7.39 (dt, $J$ = 1.6, 1.7 Hz, 1H), 7.16 (dd, $J$ = 4.8, 4.9 Hz, 1H), 7.02 (d, $J$ = 5.9 Hz, 2H), 3.89 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 149.19, 149.05, 147.63, 147.25, 135.37, 133.37, 123.03, 122.60, 37.30; HRMS (ESI) calcd for $C_{11}H_{10}N_2$ $(M + H)^+$ 171.0924, found 171.0910.

**5-(pyridin-4-ylmethyl)pyrimidine (3at)**

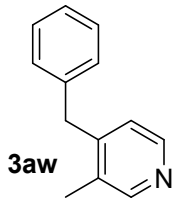


3at

*Compound **3at***: 19 mg, 23% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 9.07 (s, 1H), 8.53 (s, 2H), 8.50 (dd, $J$ = 6.0, 3.2 Hz, 2H), 7.04 (d, $J$ = 5.8 Hz, 2H), 3.91 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 156.46, 156.07, 149.35, 146.13, 131.33, 122.88, 34.82; HRMS (ESI) calcd for $C_{10}H_{10}N_3$ $(M + H)^+$

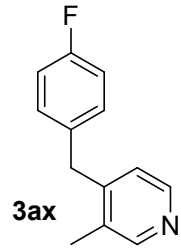
172.0876, found 172.0871.

**4-benzyl-3-methylpyridine (3aw)**[10]



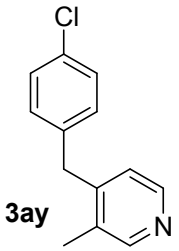

*Compound **3aw***: 46 mg, 51% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.30 (s, 1H), 8.28 (d, $J$ = 5.0 Hz, 1H), 7.22 (t, $J$ = 7.4 Hz, 2H), 7.17 (t, $J$ = 5.9 Hz, 1H), 7.04 (d, $J$ = 7.5 Hz, 2H), 6.89 (d, $J$ = 4.9 Hz, 1H), 3.88 (s, 2H), 2.17 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 149.74, 146.84, 146.67, 137.21, 131.05, 127.85, 127.64, 125.50, 123.30, 37.69, 15.35. HRMS (ESI) calcd for $C_{13}H_{14}N$ $(M + H)^+$ 184.1128, found 184.1114.

**4-(4-fluorobenzyl)-3-methylpyridine (3ax)**




*Compound **3ax***: 57 mg, 57% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.29 (d, $J$ = 7.4 Hz, 2H), 6.99 (t, $J$ = 6.8 Hz, 2H), 6.91 (t, $J$ = 8.5 Hz, 2H), 6.87 (d, $J$ = 4.9 Hz, 1H), 3.85 (s, 2H), 2.16 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 149.82, 146.75, 146.63, 131.90 (d, $J$ = 113.4 Hz), 129.2963, 129.2179, 127.75 (d, $J$ = 21.2 Hz), 123.15, 114.59, 114.38, 36.88, 15.31; $^{19}$F NMR (375 MHz, $CDCl_3$): $\delta$ -116.43. HRMS (ESI) calcd for $C_{13}H_{13}FN$ $(M + H)^+$ 202.1034, found 202.1011.

**4-(4-chlorobenzyl)-3-methylpyridine (3ay)**




*Compound **3ay***: 60 mg, 56% yield, colorless oil; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.29 (d, $J$ = 7.7 Hz, 2H), 7.18 (d, $J$ = 8.0 Hz, 2H), 6.95 (d, $J$ = 8.0 Hz, 2H), 6.87 (d, $J$ = 4.9 Hz, 1H), 3.84 (s, 2H), 2.14 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 149.84, 146.75, 146.28, 135.67, 131.40, 130.99, 129.15, 127.79, 123.19, 37.04, 15.32. HRMS (ESI) calcd for $C_{13}H_{13}ClN$ $(M + H)^+$ 218.0738, found 218.0726.

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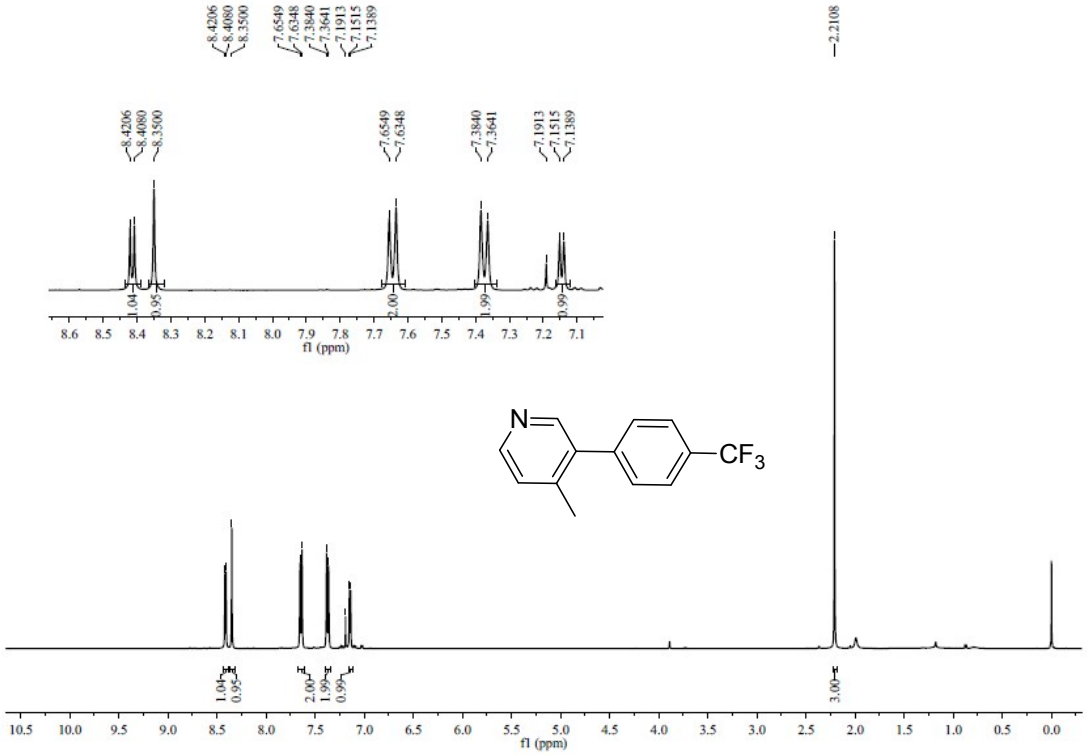
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8.3500
7.6549
7.6348
7.3840
7.3641
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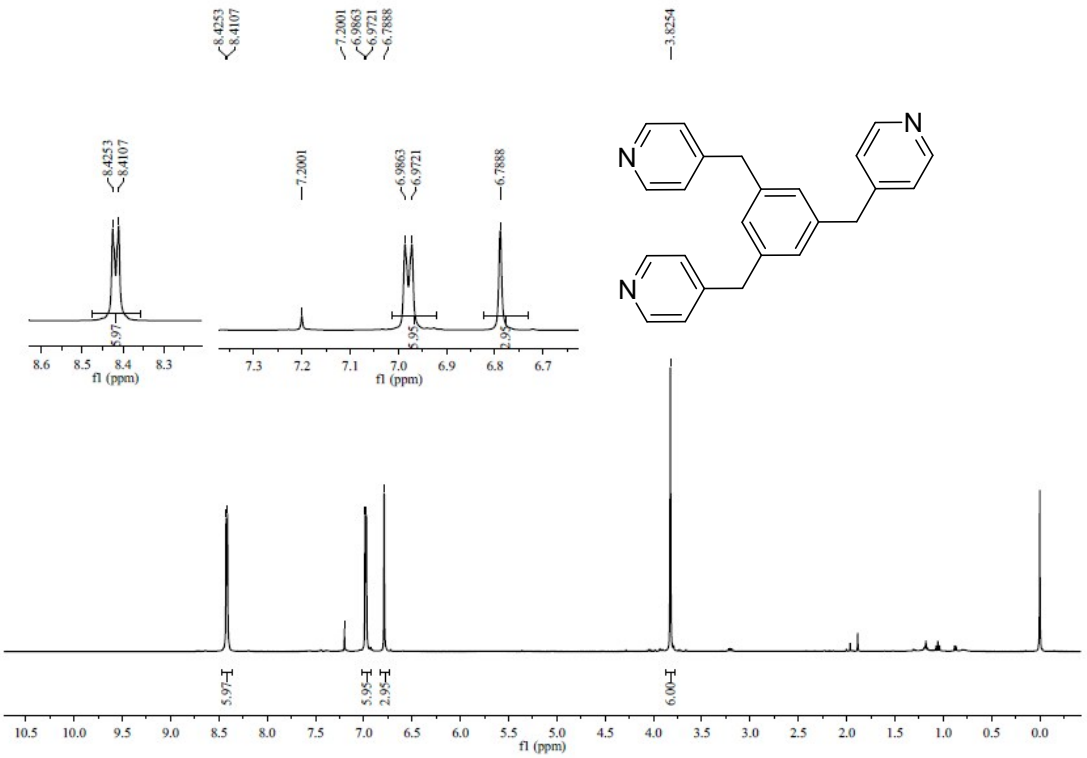
7.1515
7.1389
2.2108
1.04
0.95
2.00
1.99
0.99
3.00
N
CF3
f1 (ppm)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6.9721
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N
N
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5.95
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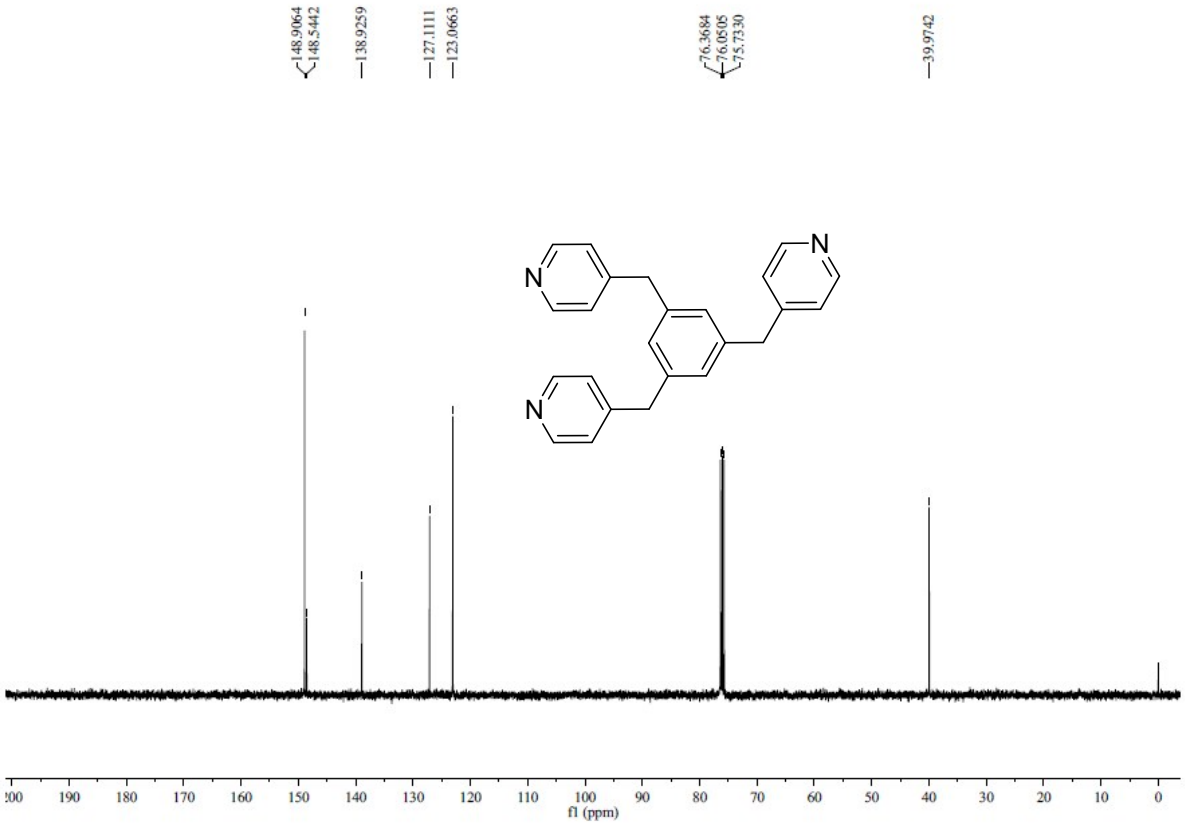
fl (ppm)
5.97
5.95
2.96
6.00
fl (ppm)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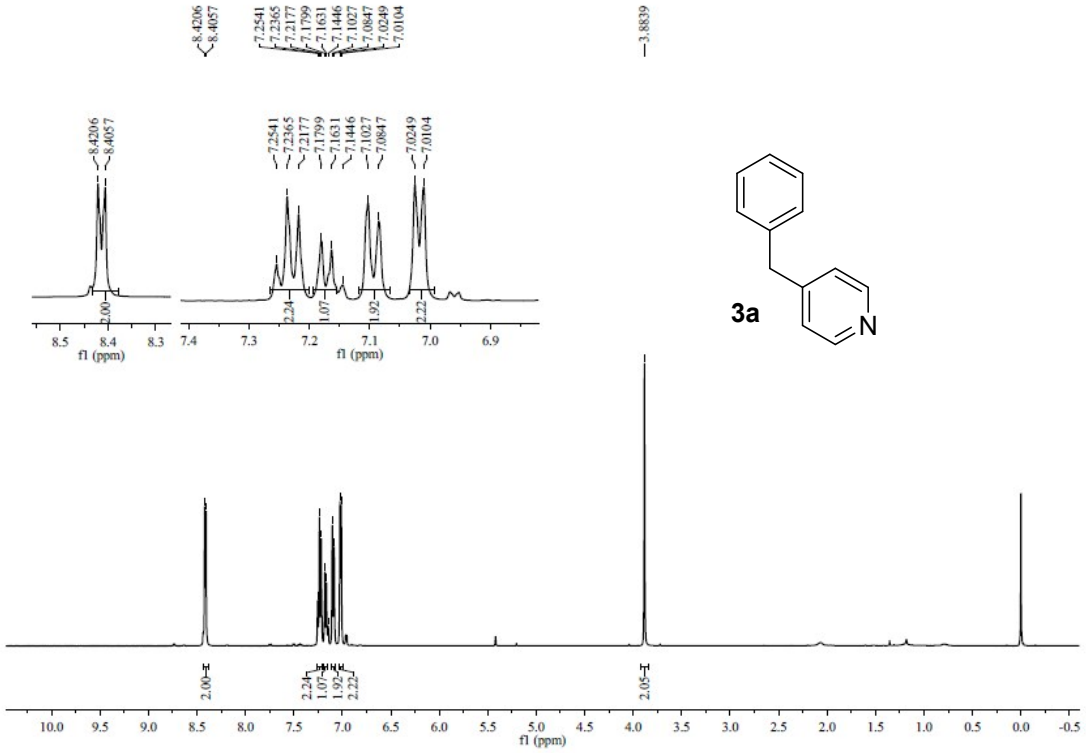
N
N
fl (ppm)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2.24
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2.22
2.05
f1 (ppm)
3a
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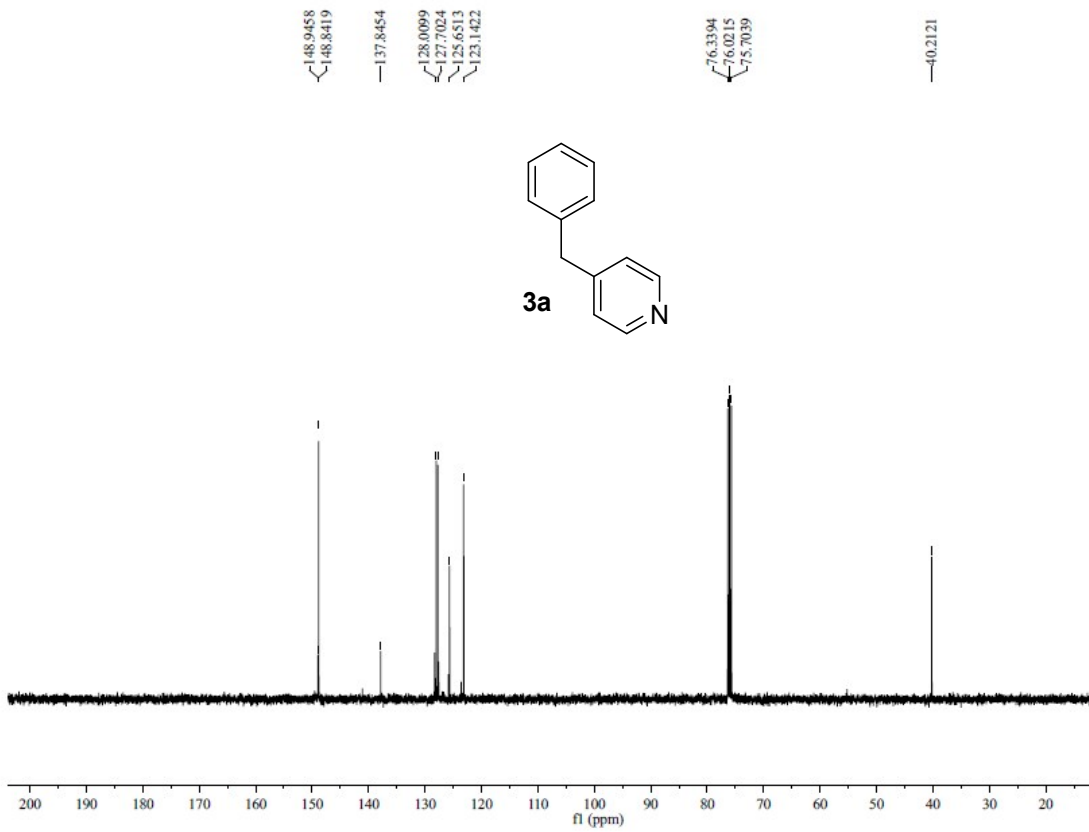
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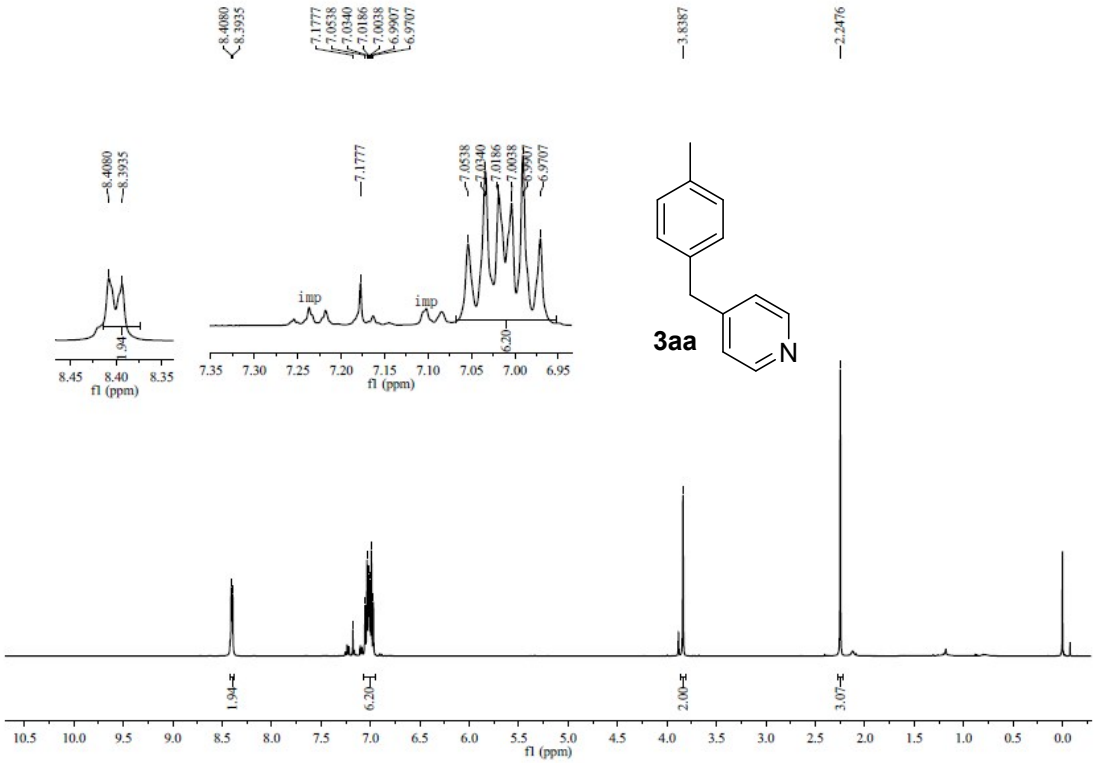
f1 (ppm)
3a
N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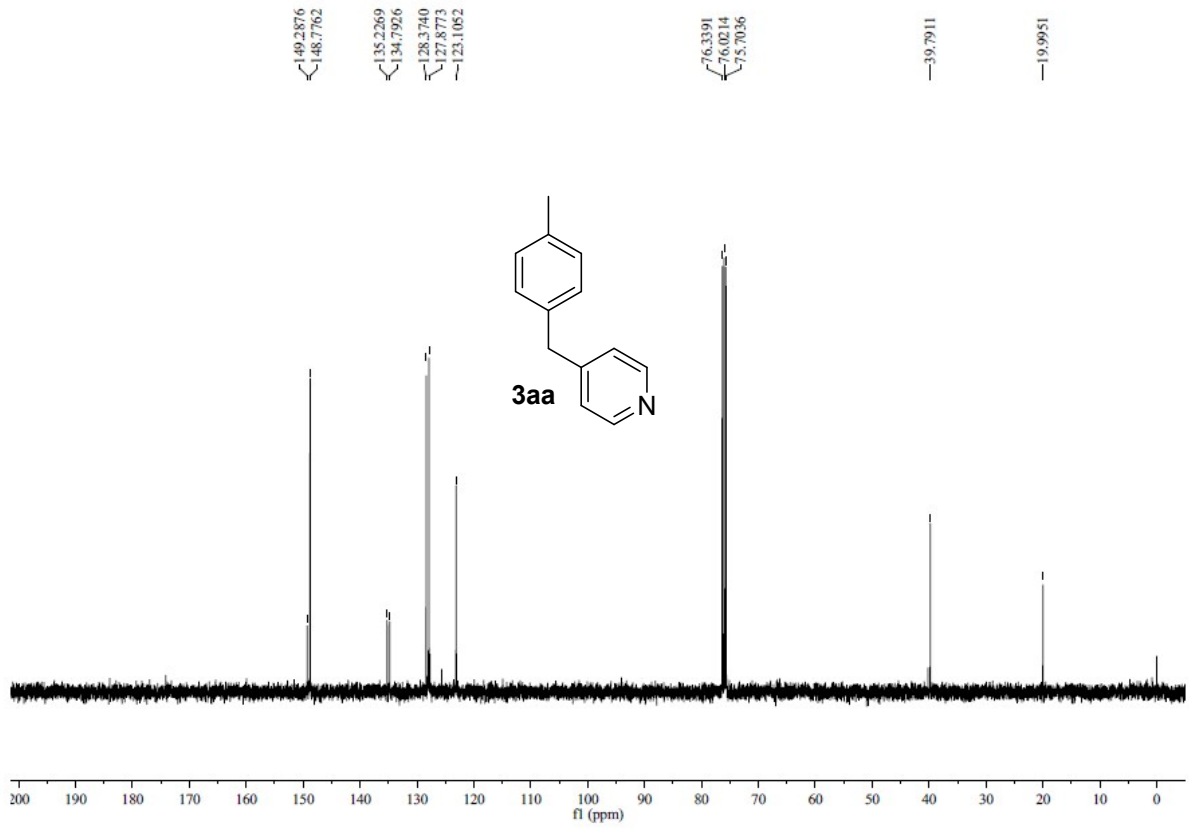
fl (ppm)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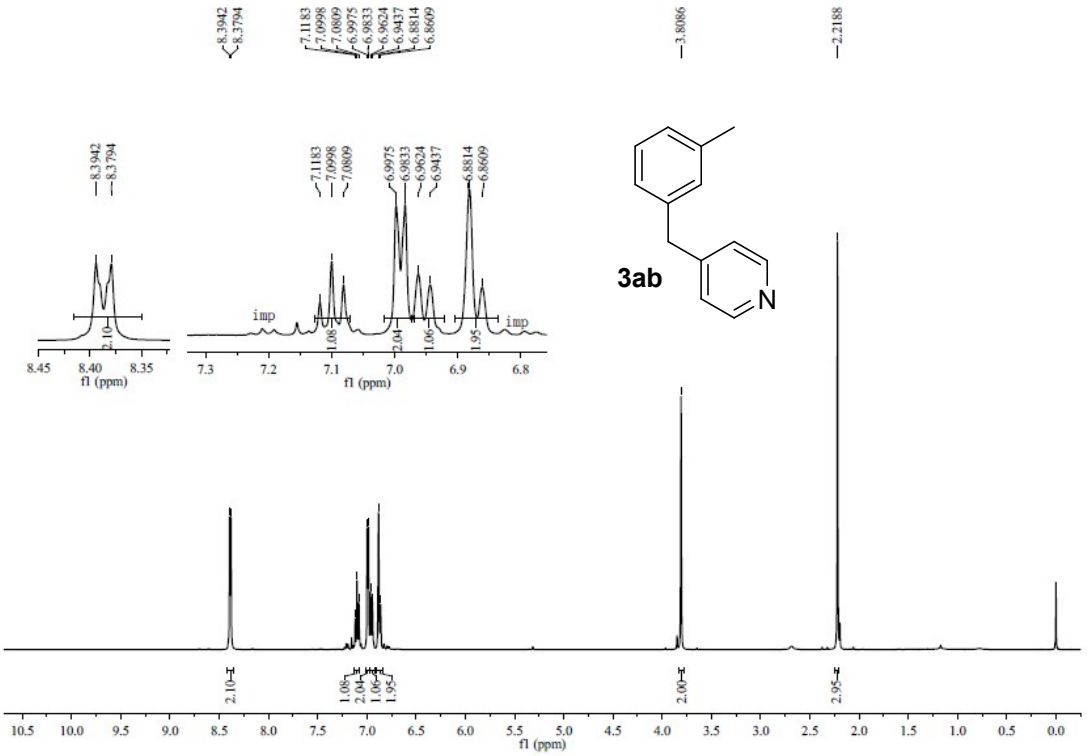
fl (ppm)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imp
imp
3ab
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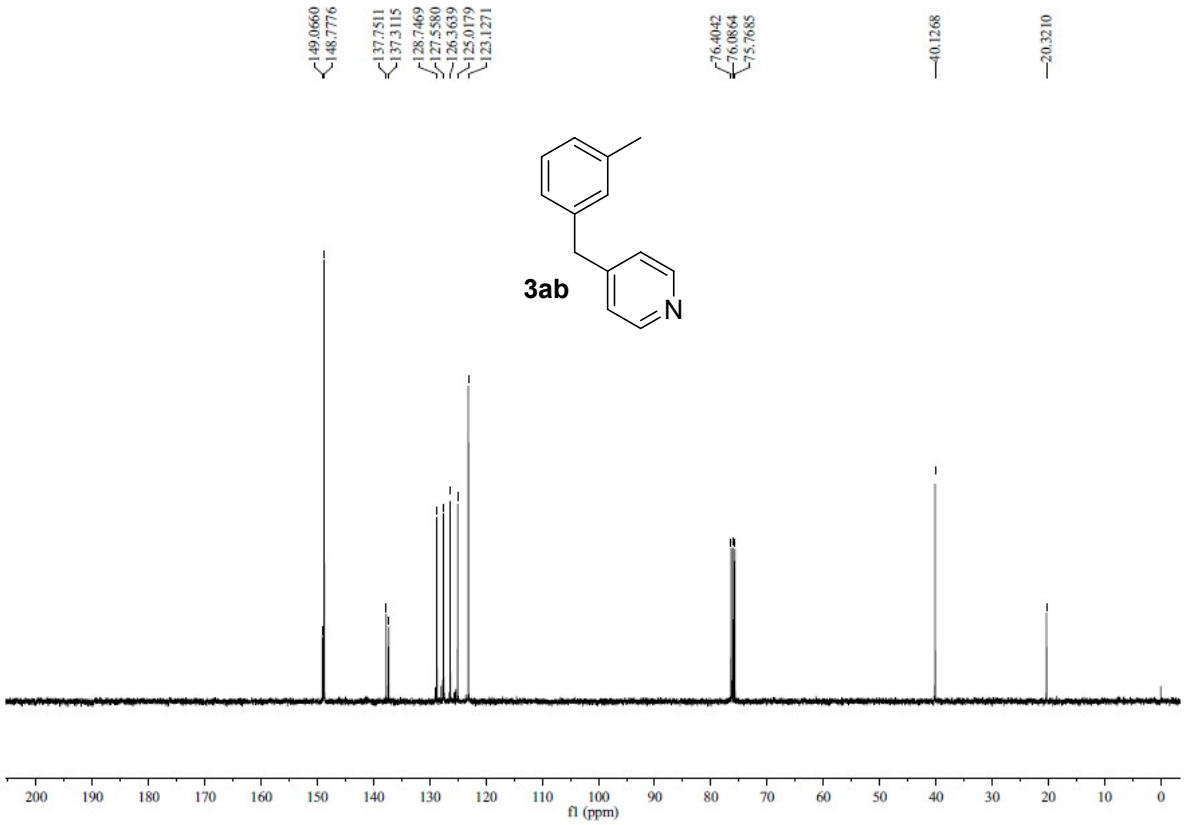
fl (ppm)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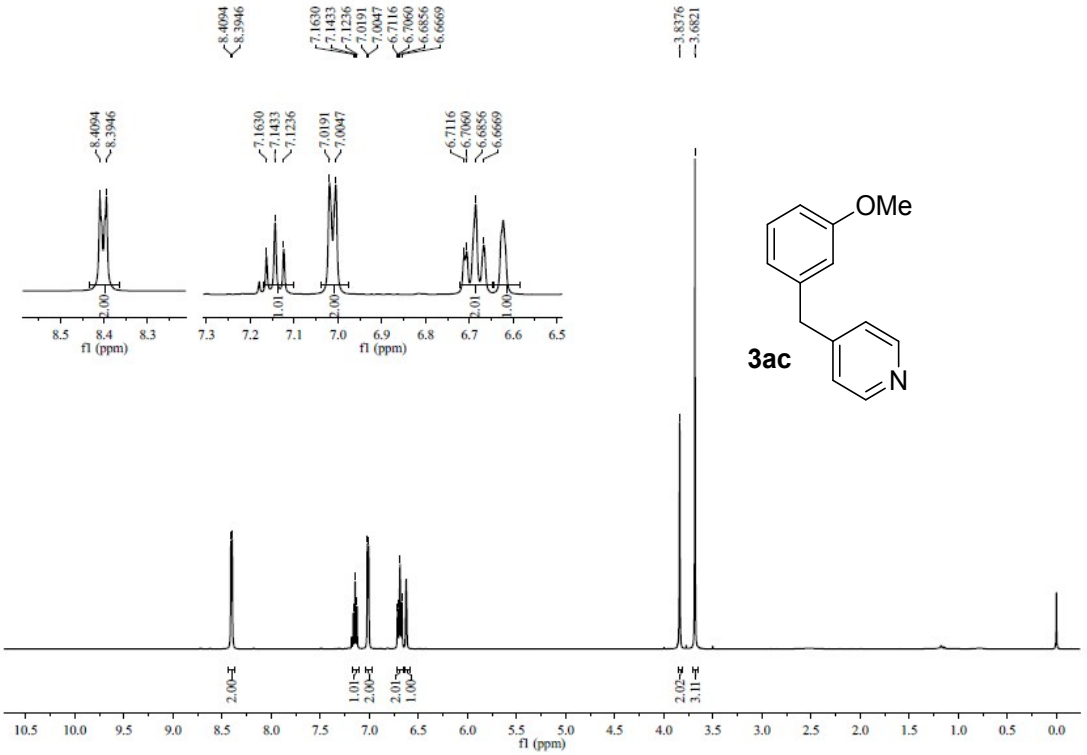
3ab
N
fl (ppm)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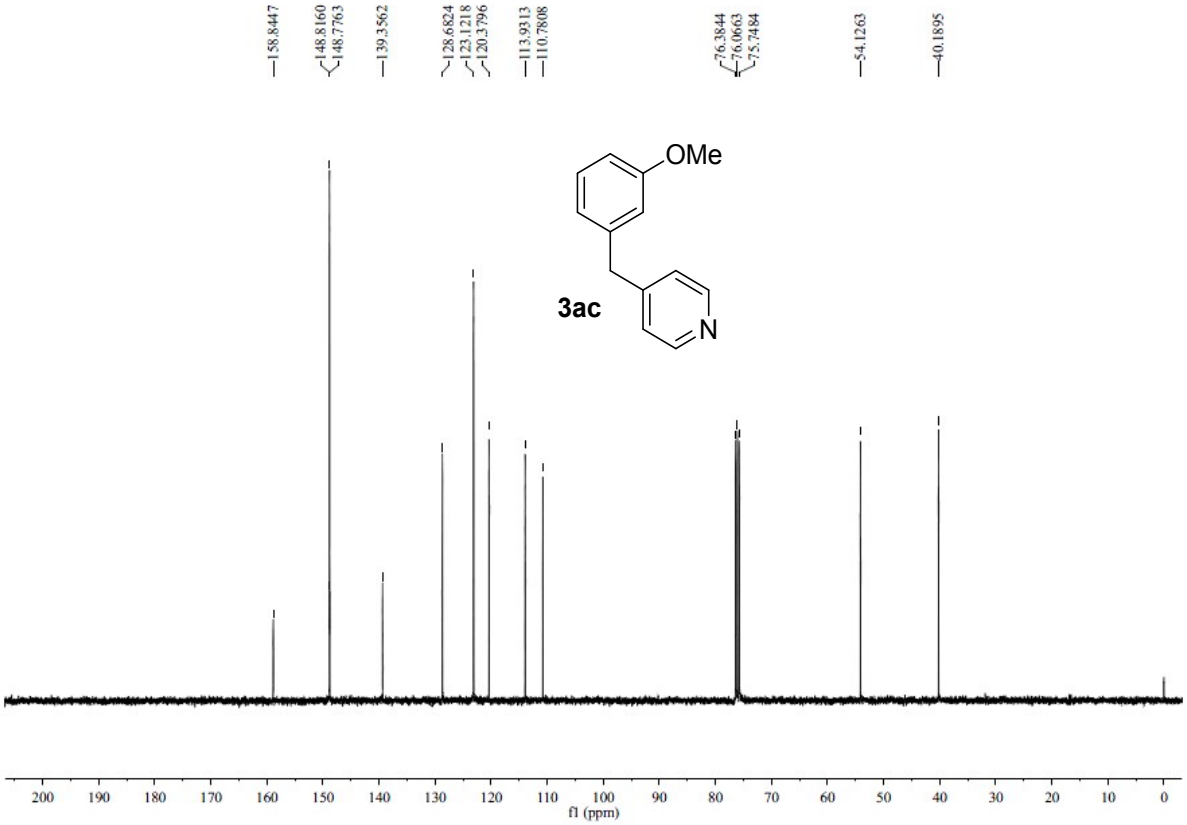
fl (ppm)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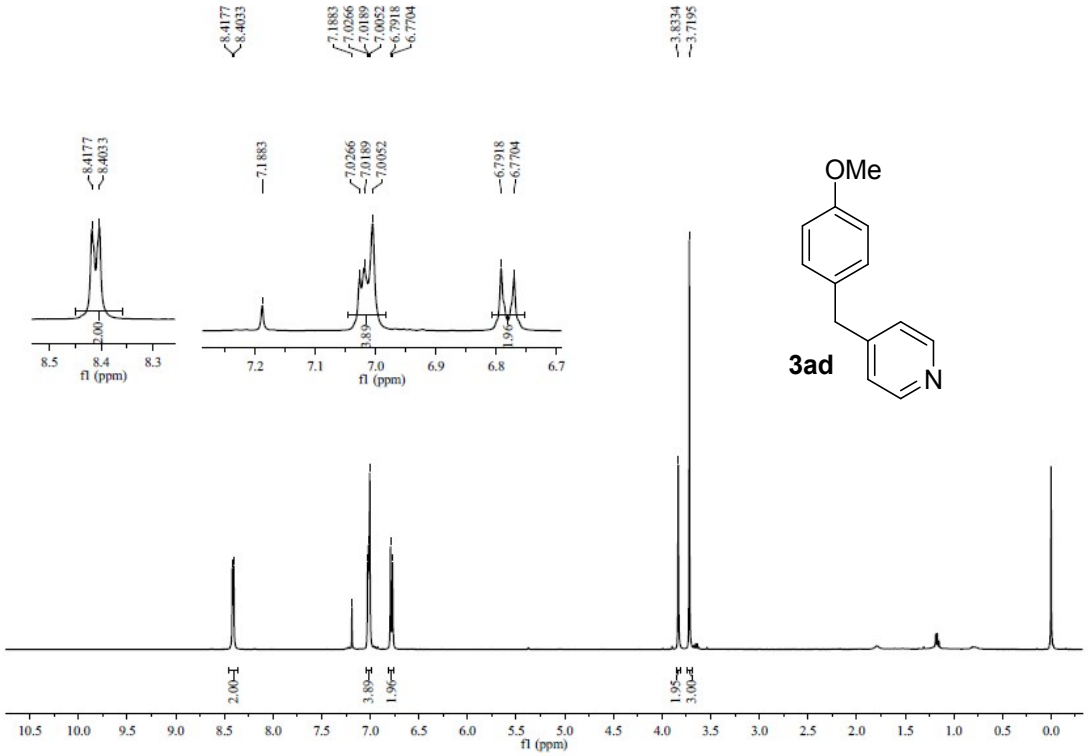
fl (ppm)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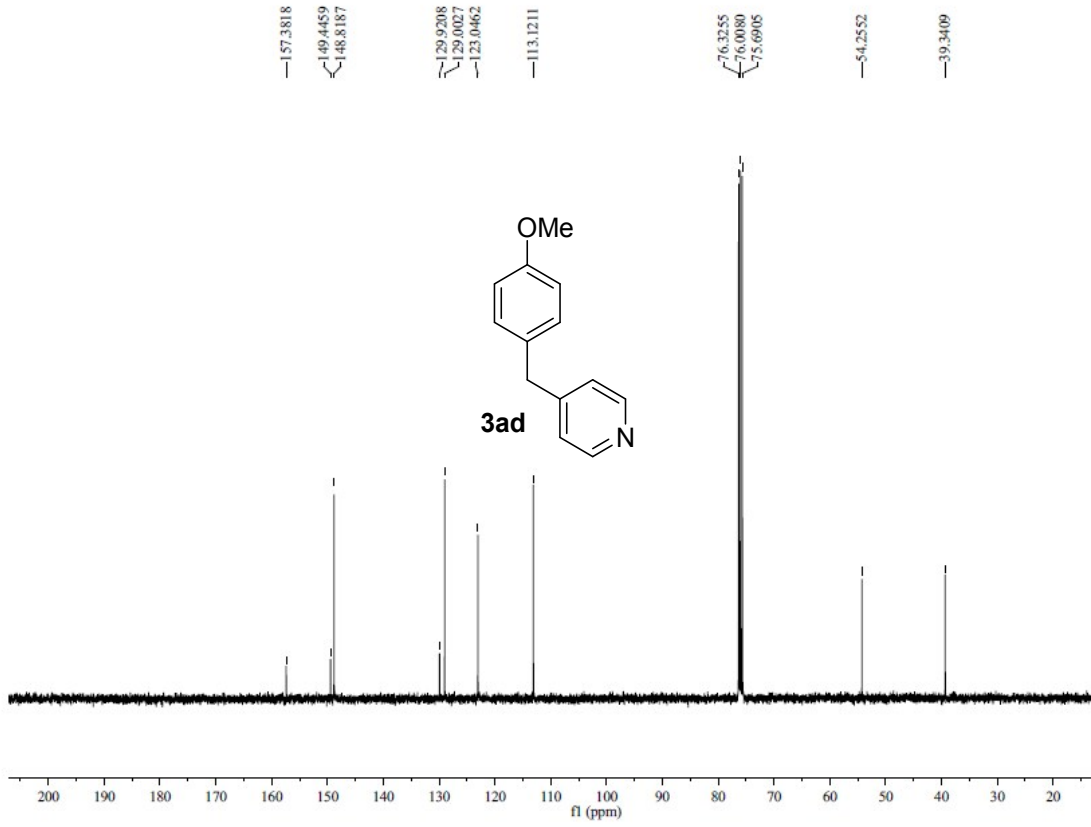
f1 (ppm)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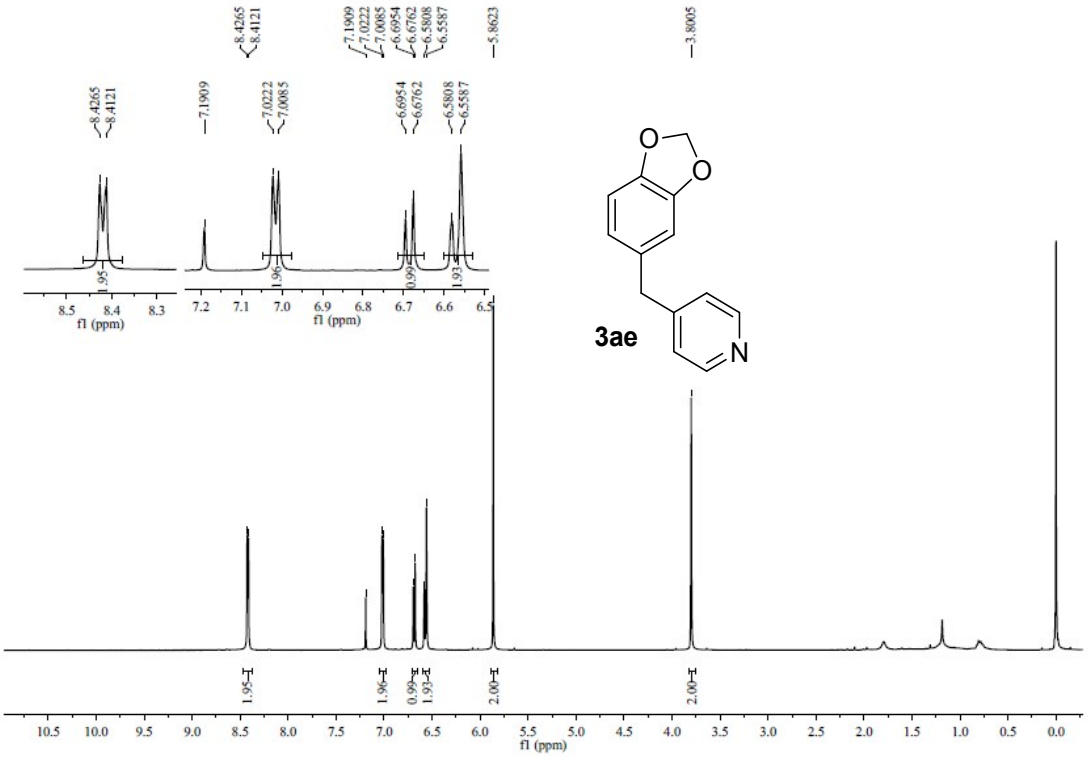
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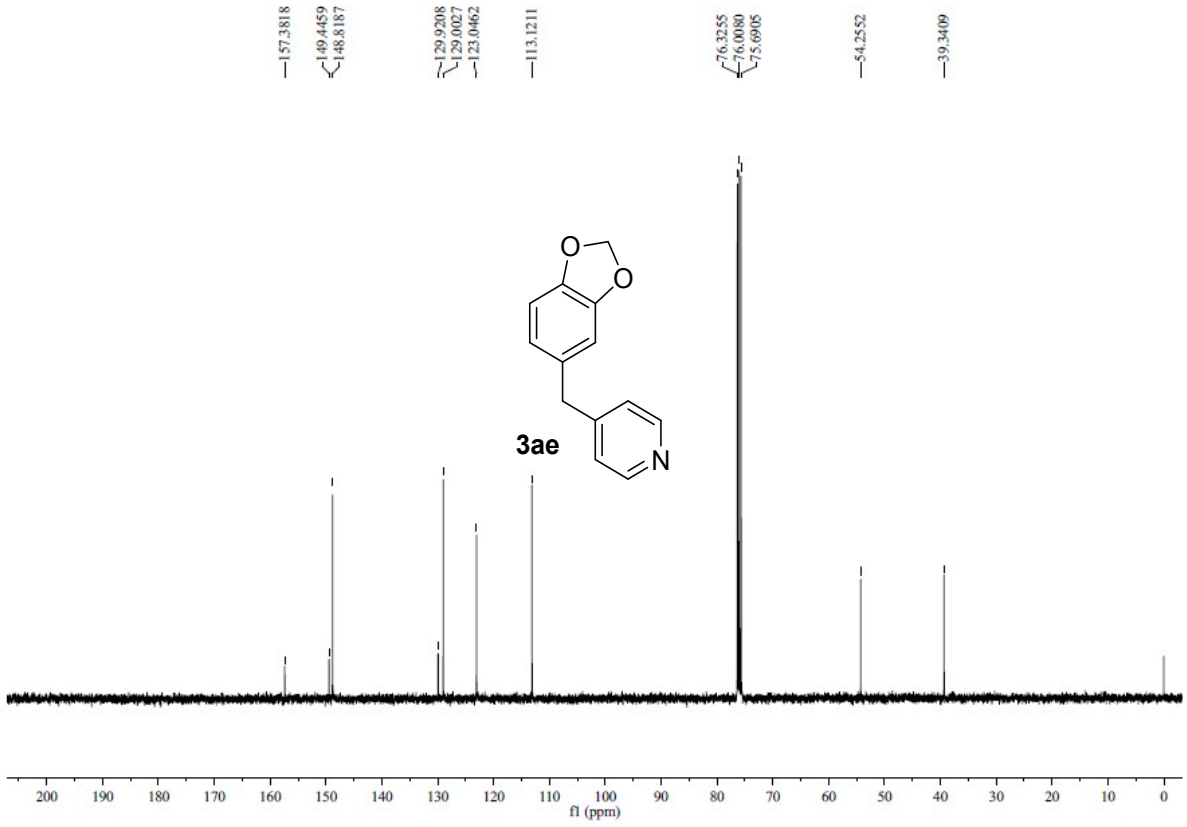
O
N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fl (ppm)
3ae
O
O
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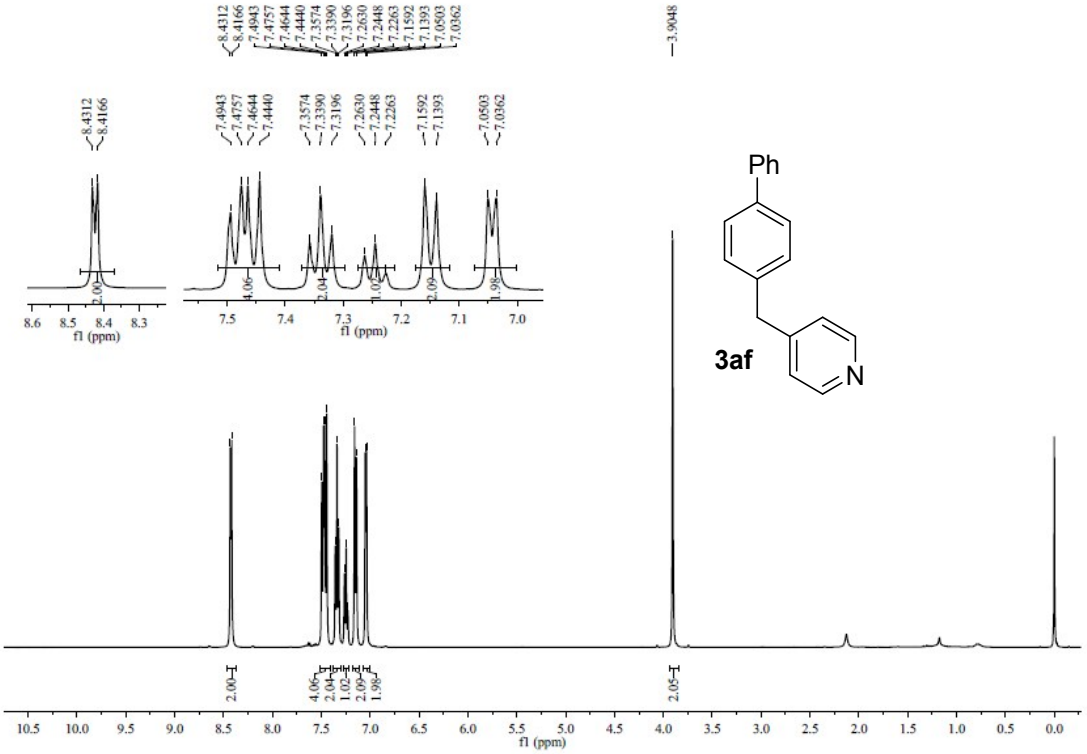
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7.4644
7.4440
7.3574
7.3390
7.3196
7.2630
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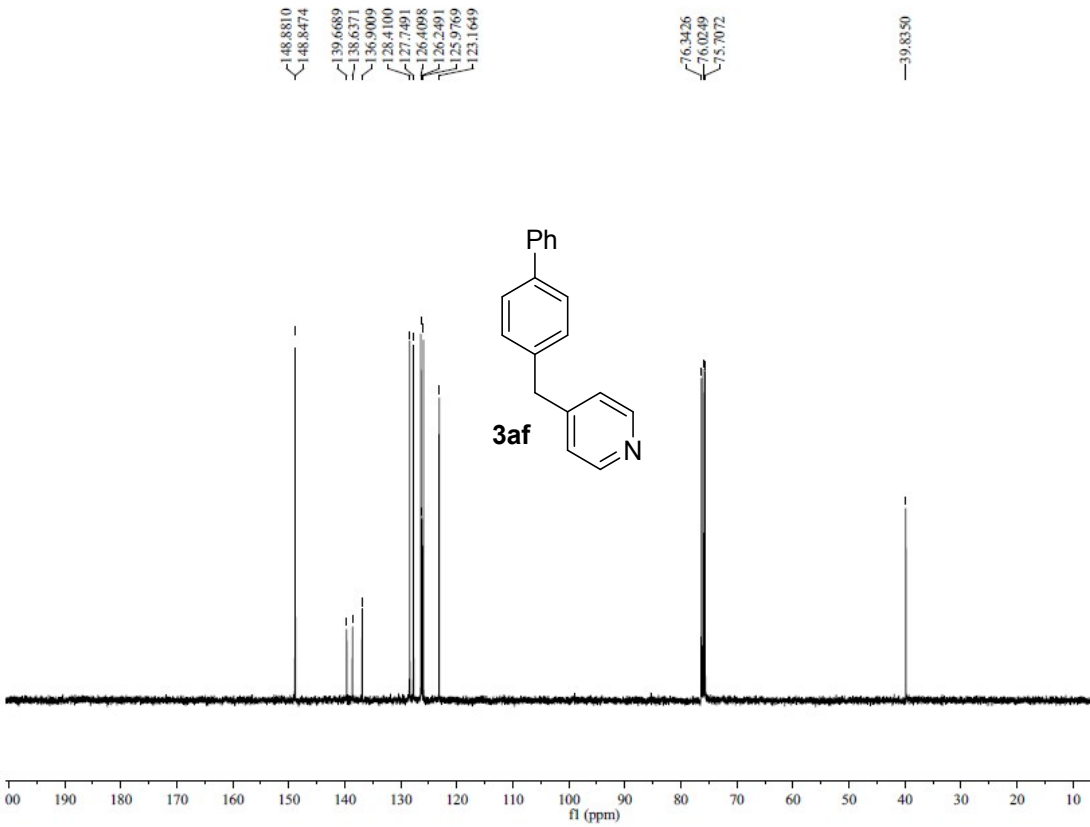
7.1592
7.1393
7.0503
7.0362
3.9048
Ph
3af
N
fl (ppm)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138.6371
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128.4100
127.7491
126.4098
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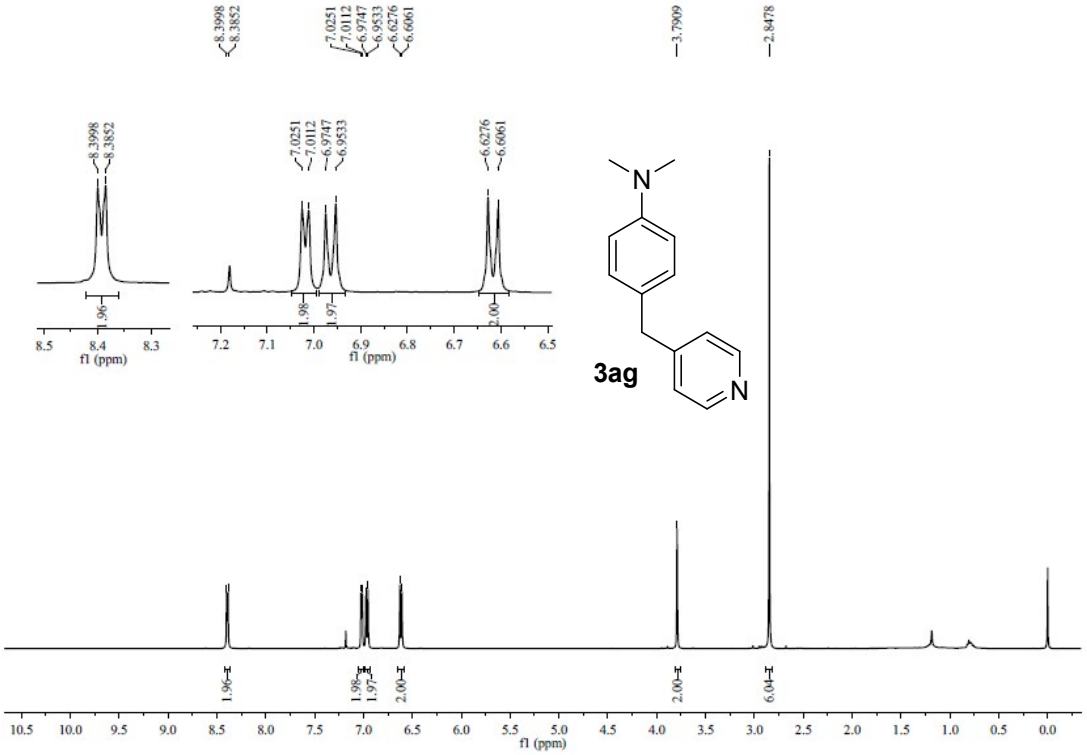
123.1649
76.3426
76.0249
75.7072
39.8350
Ph
3af
N
fl (ppm)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7.0112
6.9747
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6.6276
6.6061
3.7909
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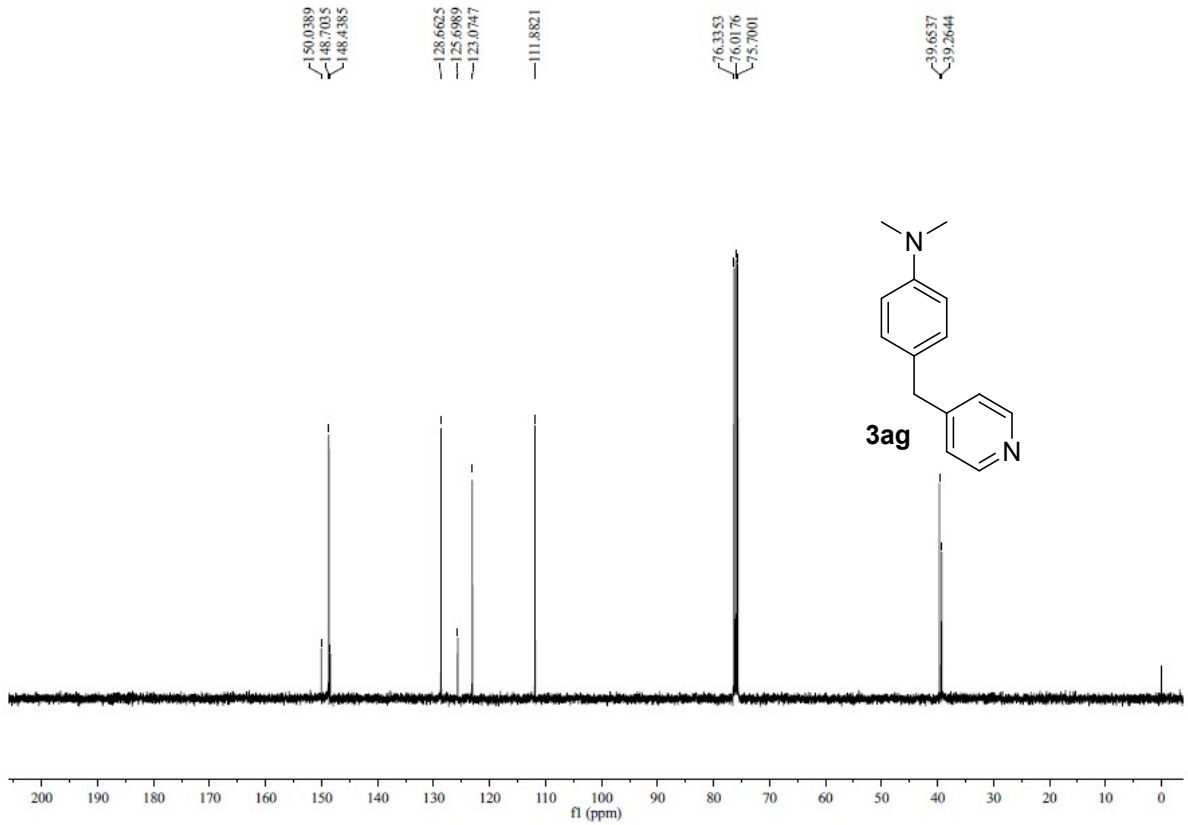
1.96
1.98
1.97
2.00
2.00
6.04
fl (ppm)
3ag
N
N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148.4385
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125.6989
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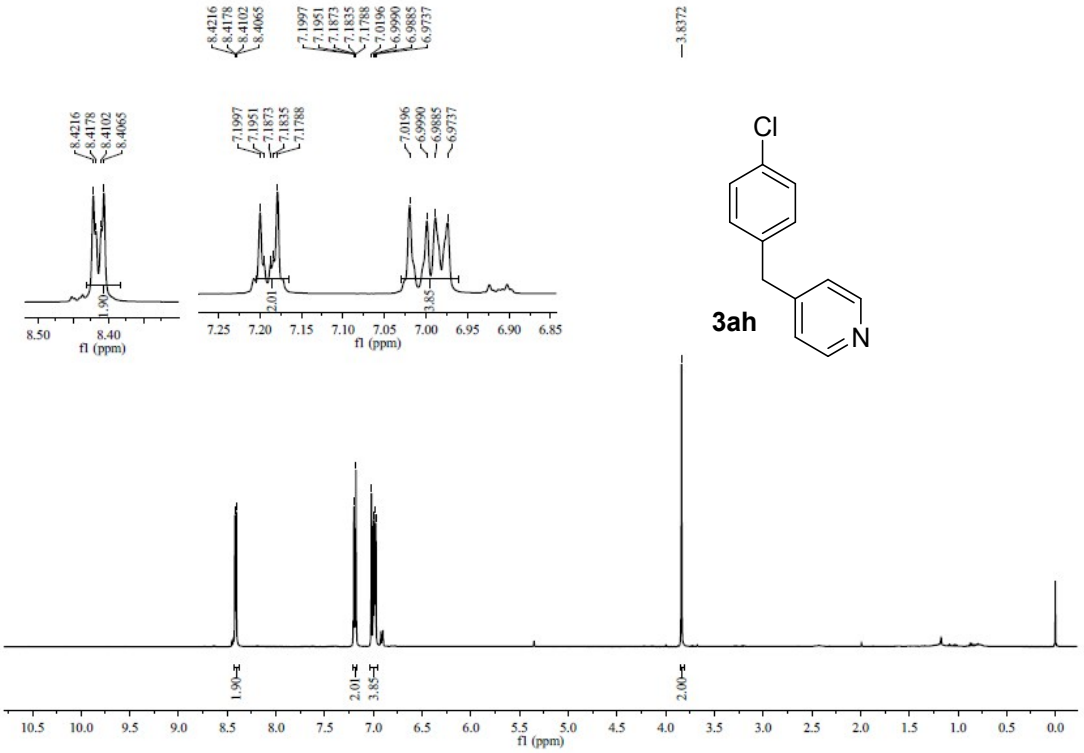
39.2644
fl (ppm)
3ag
N
N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8.4065
7.1997
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7.1873
7.1835
7.1788
7.0196
6.9990
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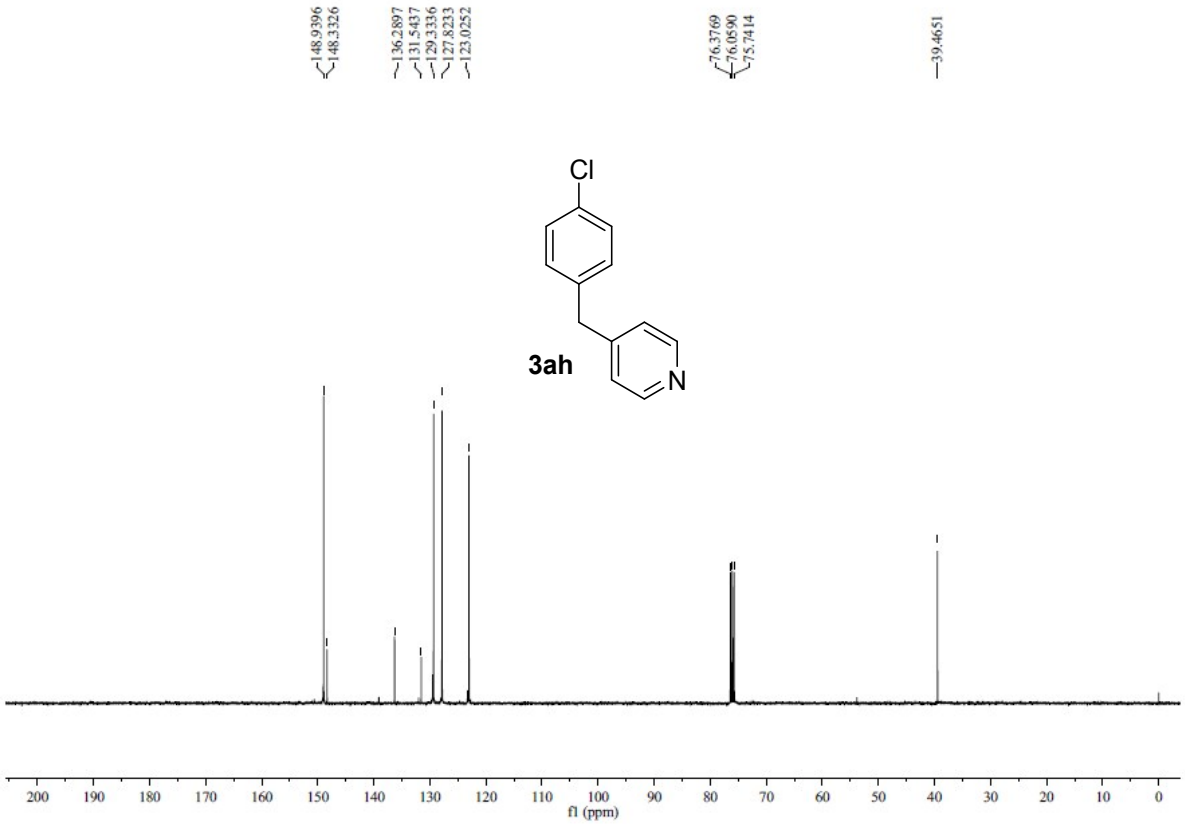
6.9737
3.8372
1.90
2.01
3.85
2.00
fl (ppm)
Cl
N
3ah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136.2897
131.5437
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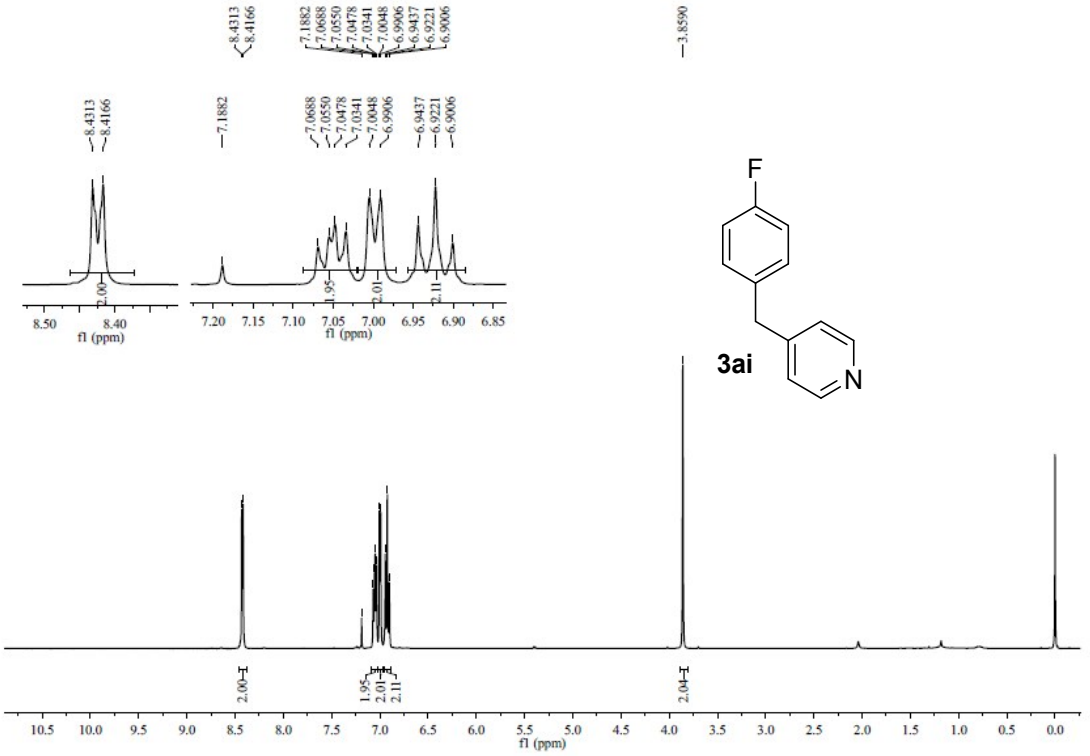
fl (ppm)
Cl
N
3ah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8.4166
7.1882
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7.0550
7.0478
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6.9006
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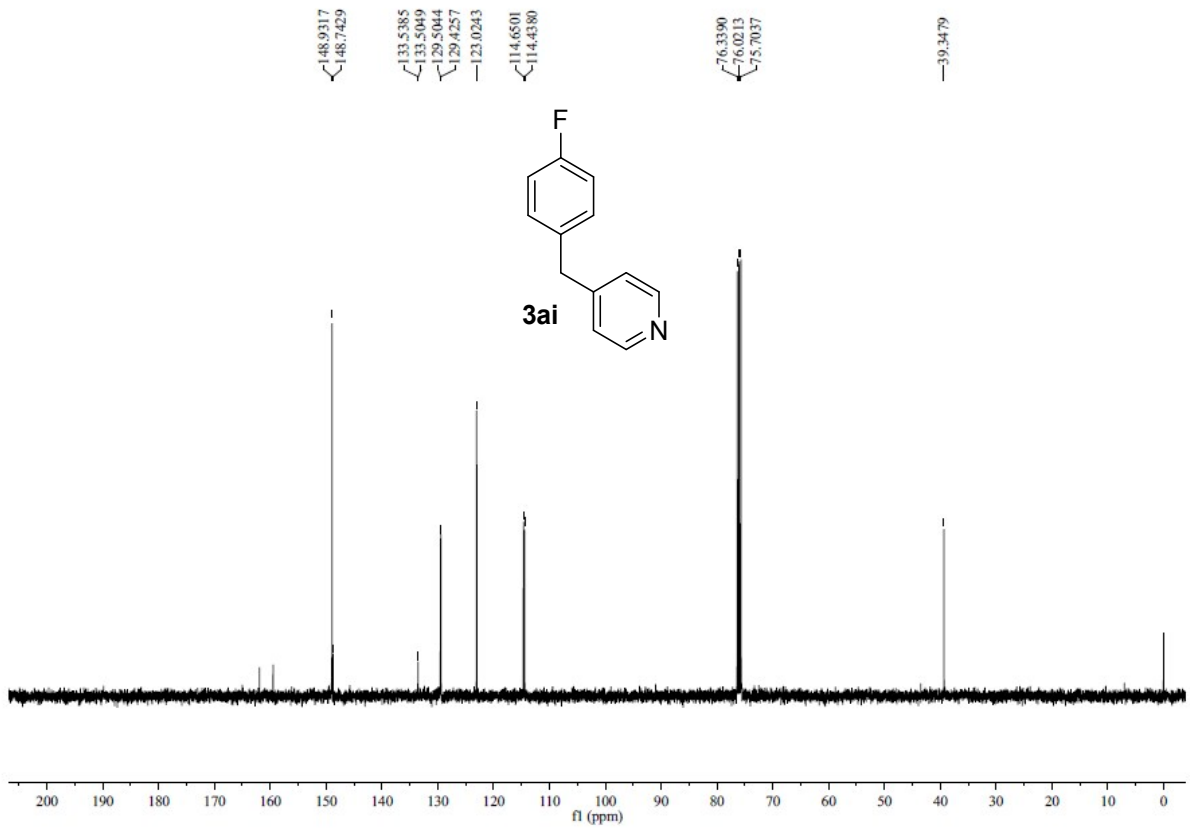
F
3ai
N
fl (ppm)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148.7429
133.5385
133.5049
129.5044
129.4257
123.0243
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75.7037
39.3479
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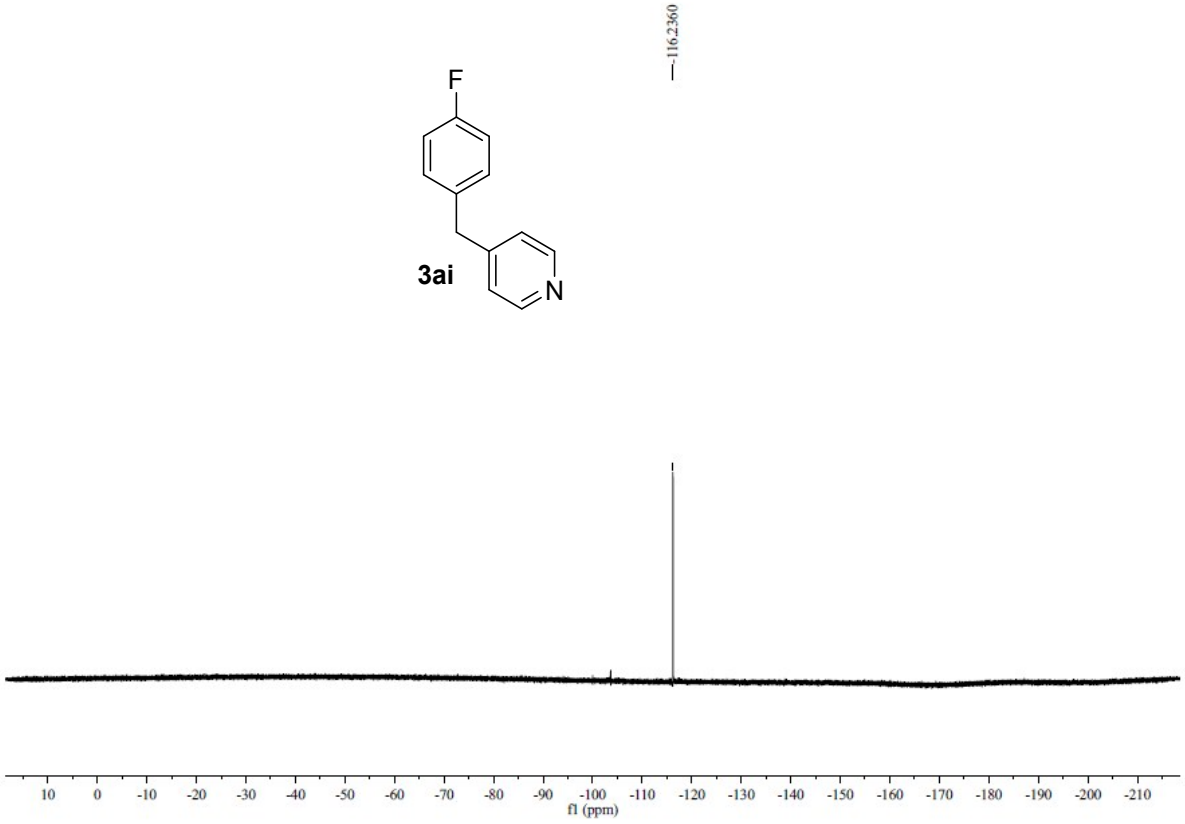
3ai
N
fl (ppm)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N
3ai
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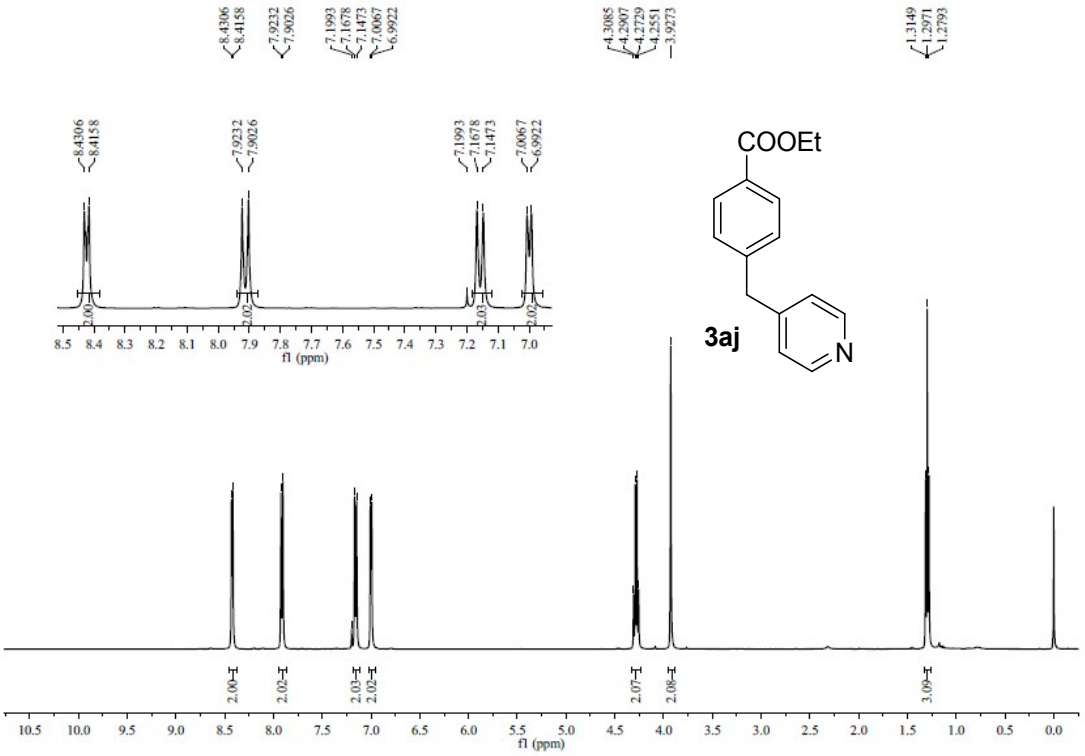
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)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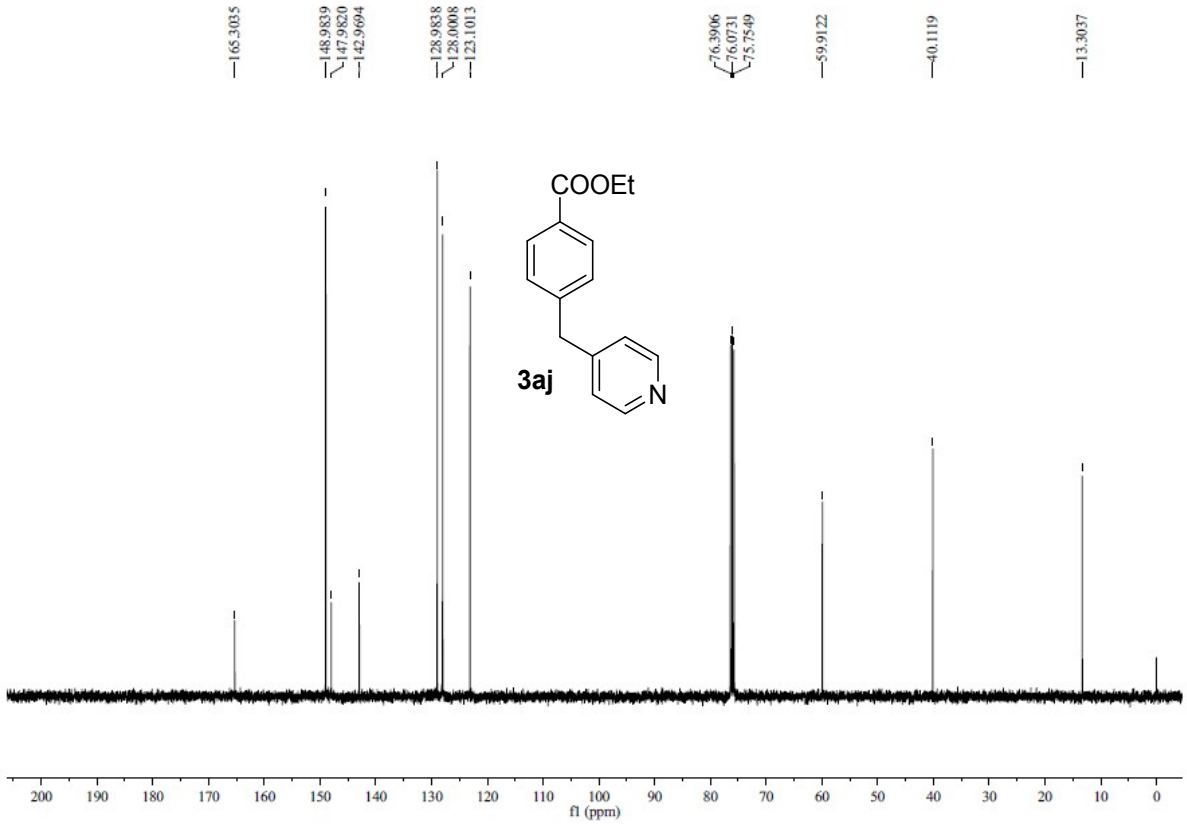
8.4158
7.9232
7.9026
7.1993
7.1678
7.1473
7.0067
6.9922
4.3085
4.2907
4.2729
4.2551
3.9273
1.3149
1.2971
1.2793
COOEt
3aj
N
fl (ppm)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147.9820
142.9694
128.9838
126.0008
123.1013
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76.0731
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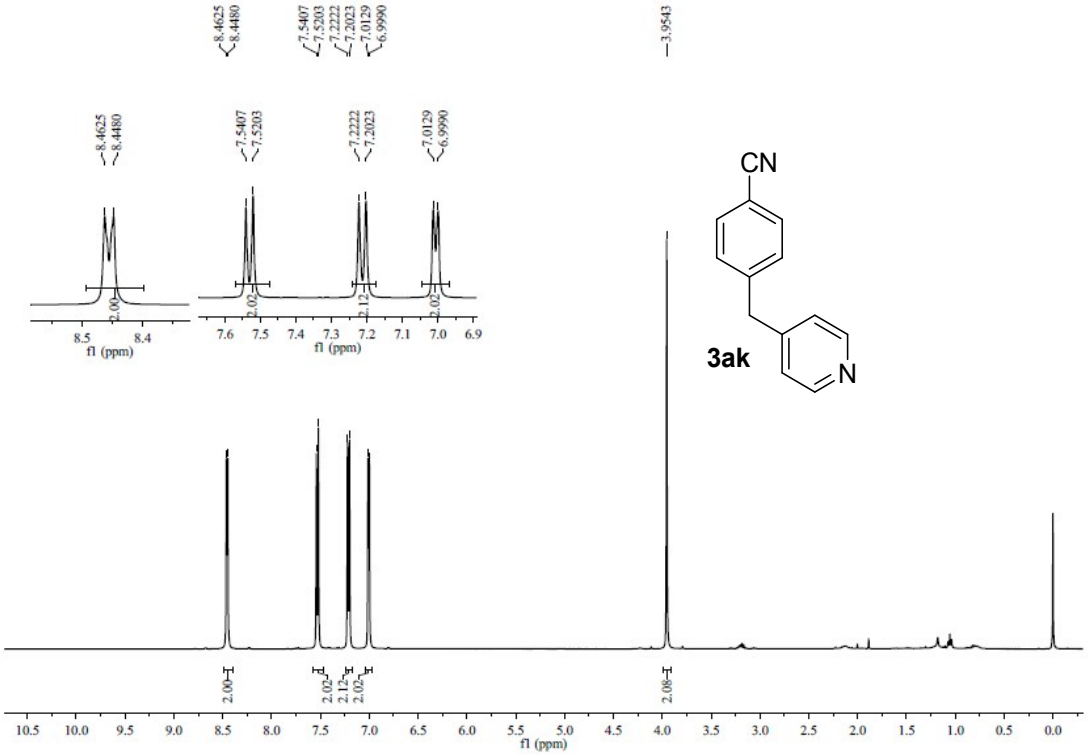
59.9122
40.1119
13.3037
COOEt
3aj
N
fl (ppm)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8.4480
7.5407
7.5203
7.2222
7.2023
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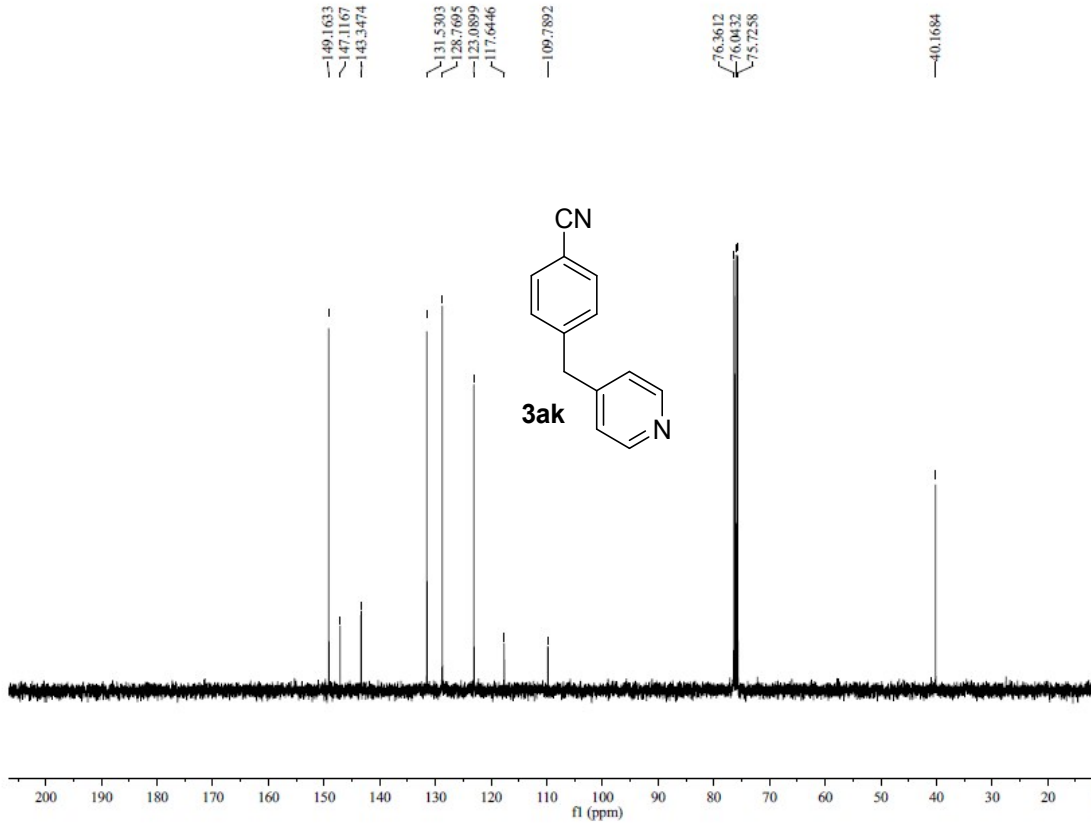
6.9990
3.9543
CN
3ak
N
f1 (ppm)
2.00
2.02
2.12
2.02
2.08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131.5303
128.7695
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76.0432
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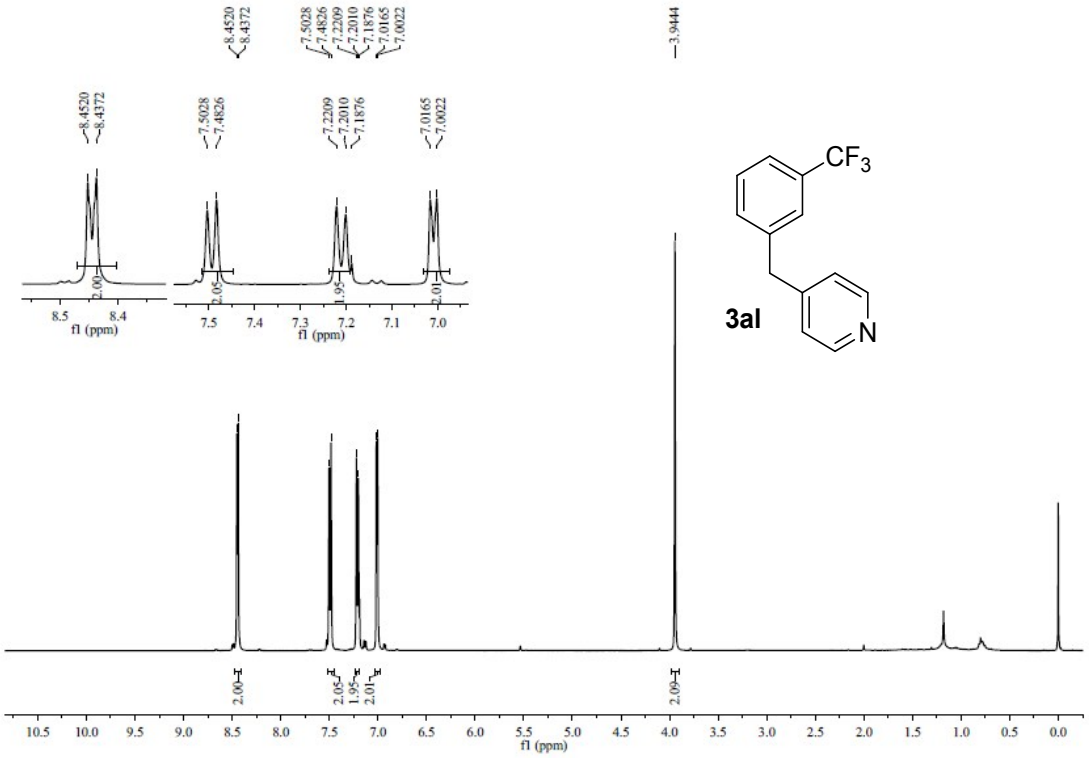
40.1684
CN
3ak
N
f1 (ppm)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7.4826
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7.2010
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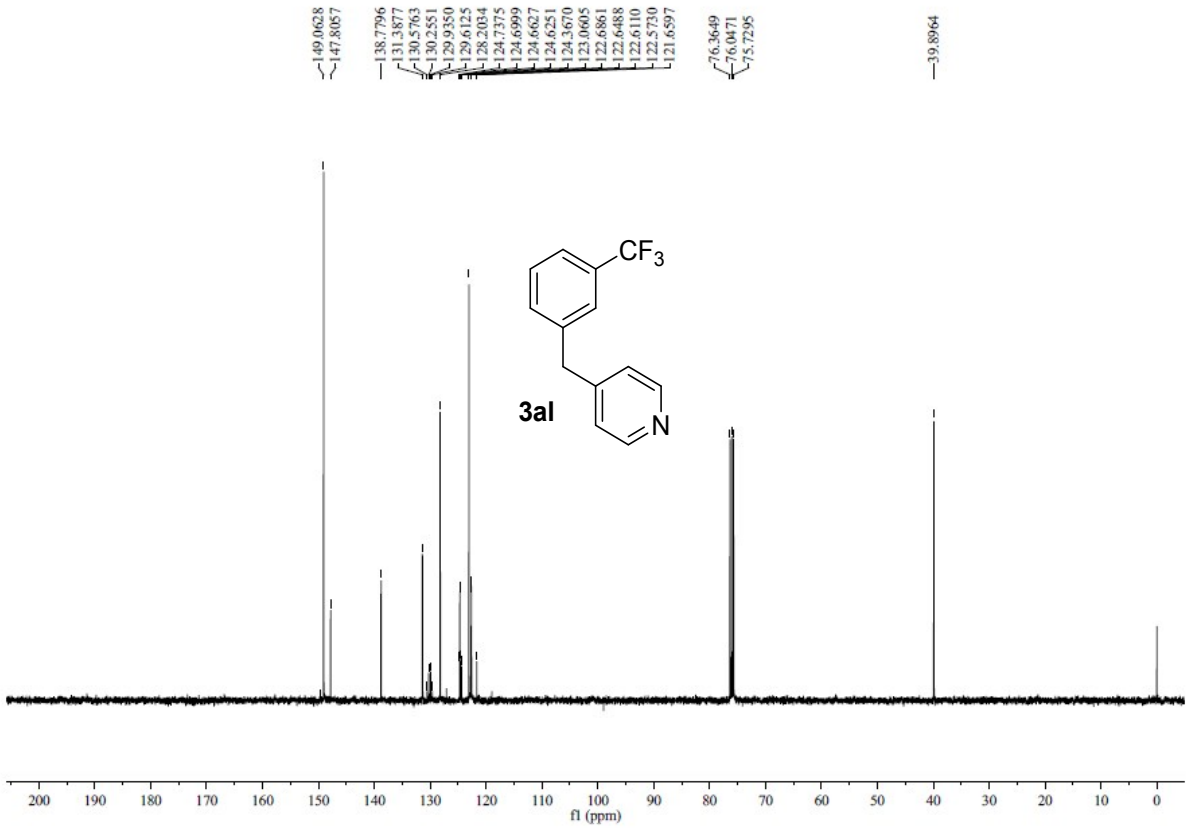
7.0165
7.0022
3.9444
CF3
N
3al
fl (ppm)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124.6251
124.3670
123.0605
122.6861
122.6488
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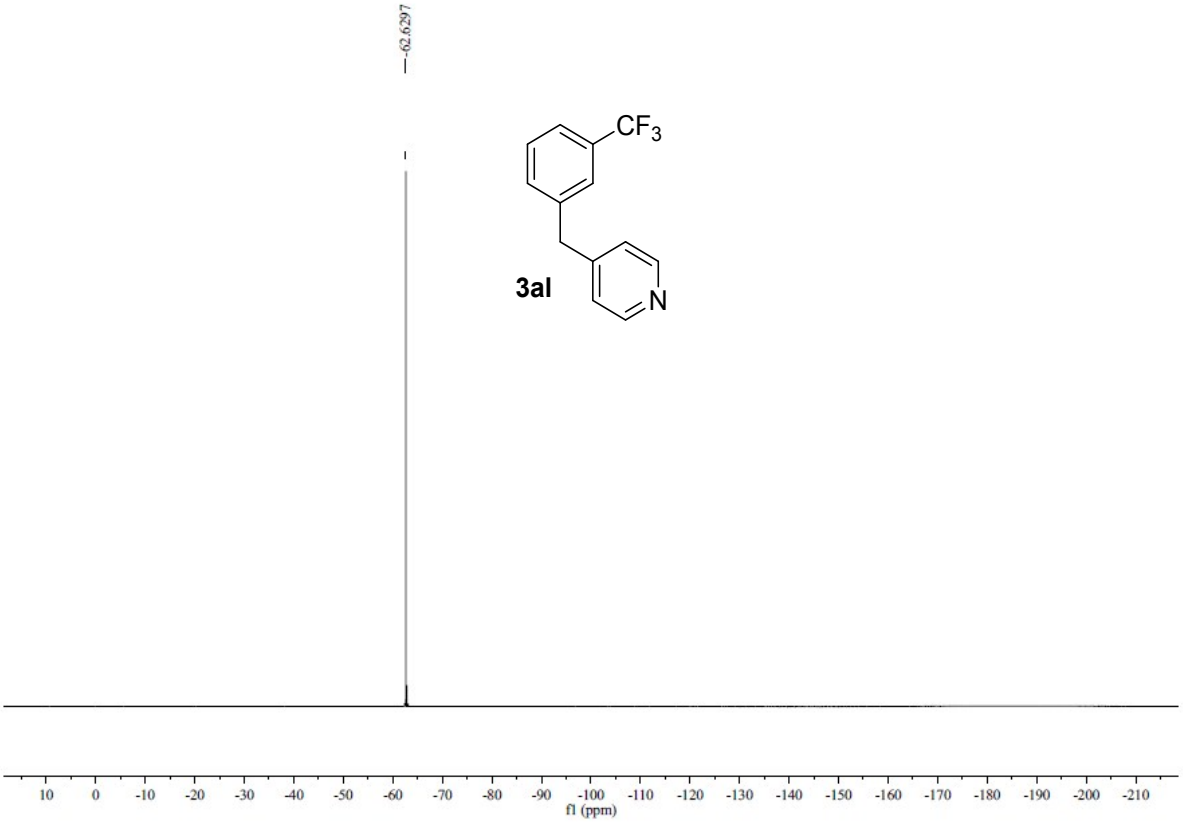
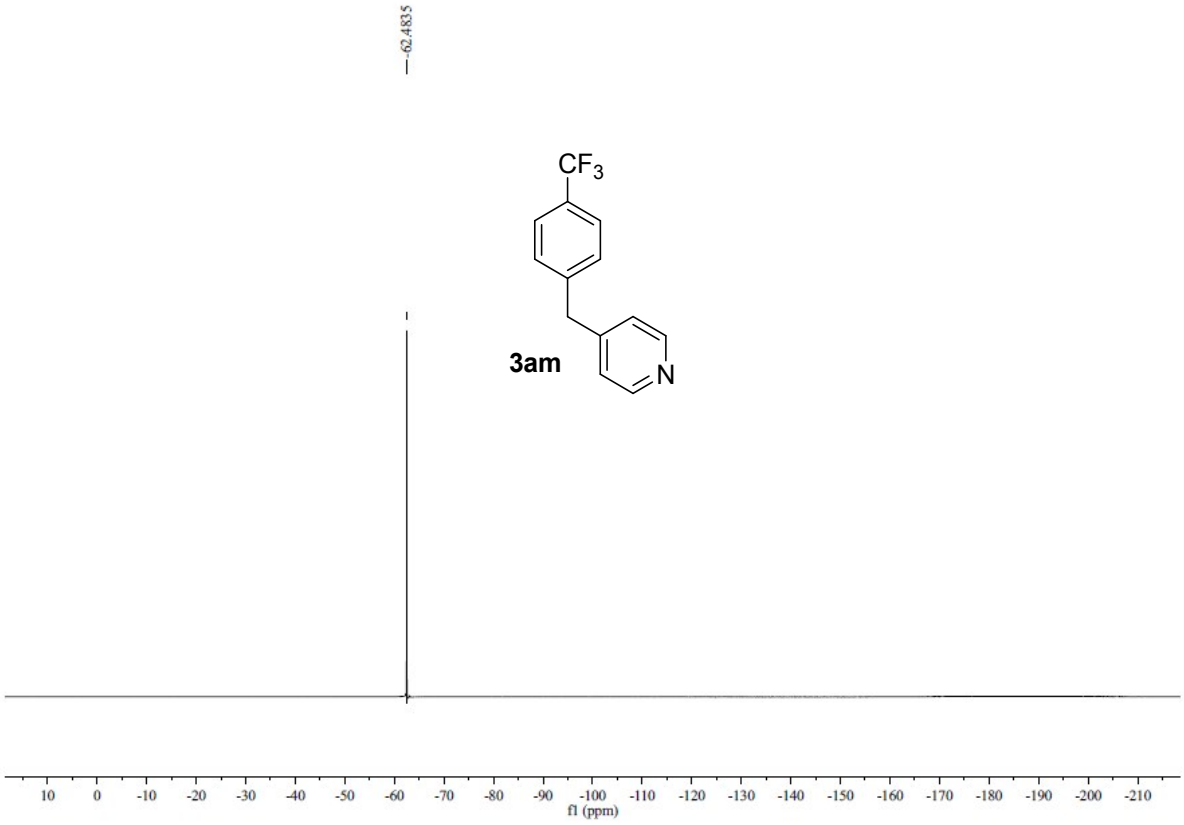
121.6597
76.3649
76.0471
75.7295
39.8964
CF3
N
3al
fl (ppm)


-62.6297
CF3
N
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

**3al**


-62.4835
CF3
N
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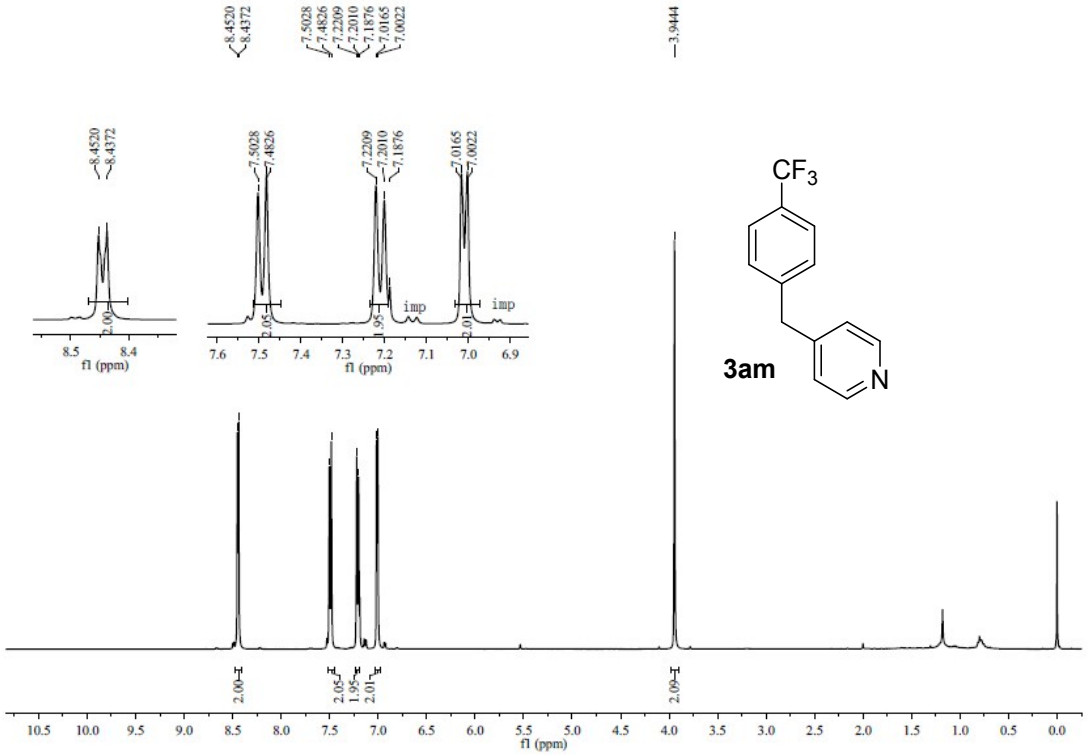
f1 (ppm)

**3am**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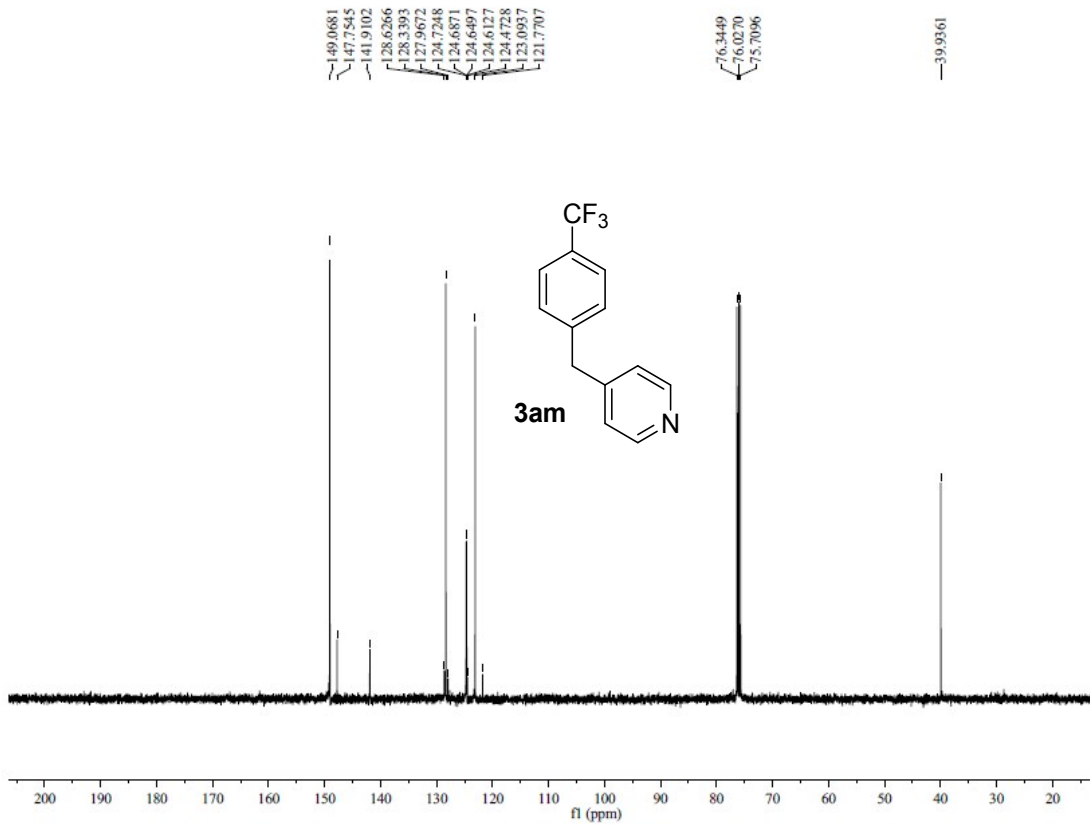
8.4372
7.5028
7.4826
7.2209
7.2010
7.1876
7.0165
7.0022
3.9444
imp
imp
CF3
N
3am
fl (ppm)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147.7545
141.9102
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128.3393
127.9672
124.7248
124.6871
124.6497
124.6127
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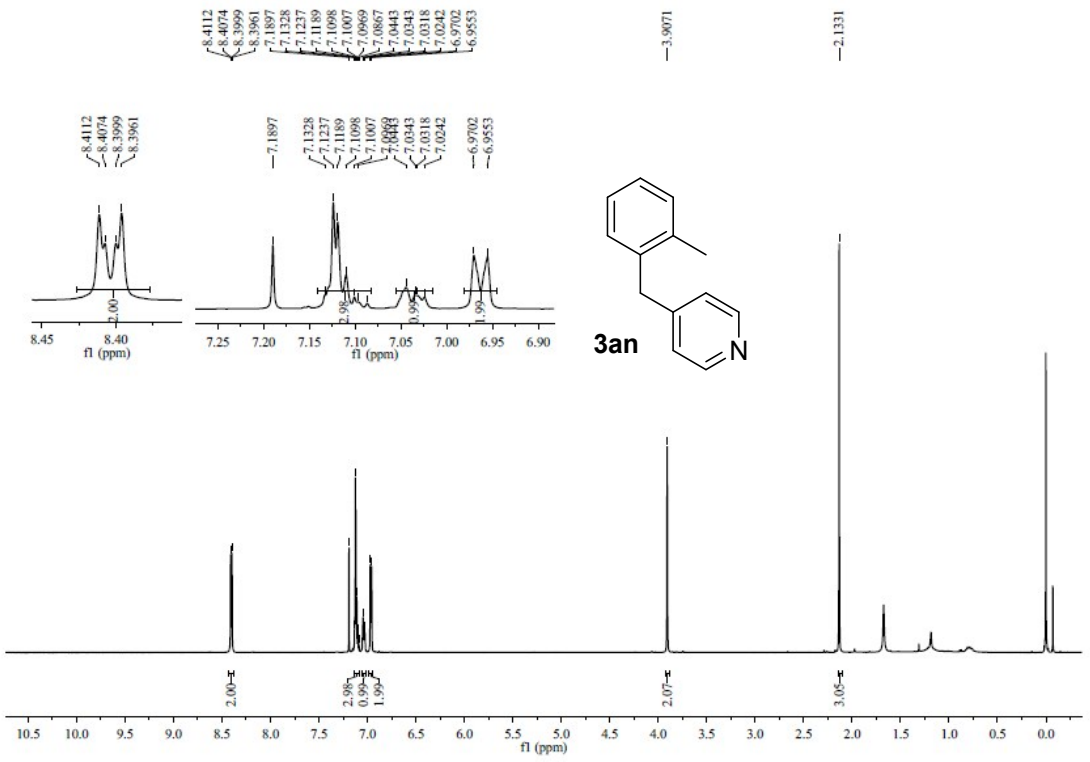
123.0937
121.7707
76.3449
76.0270
75.7096
39.9361
CF3
N
3am
fl (ppm)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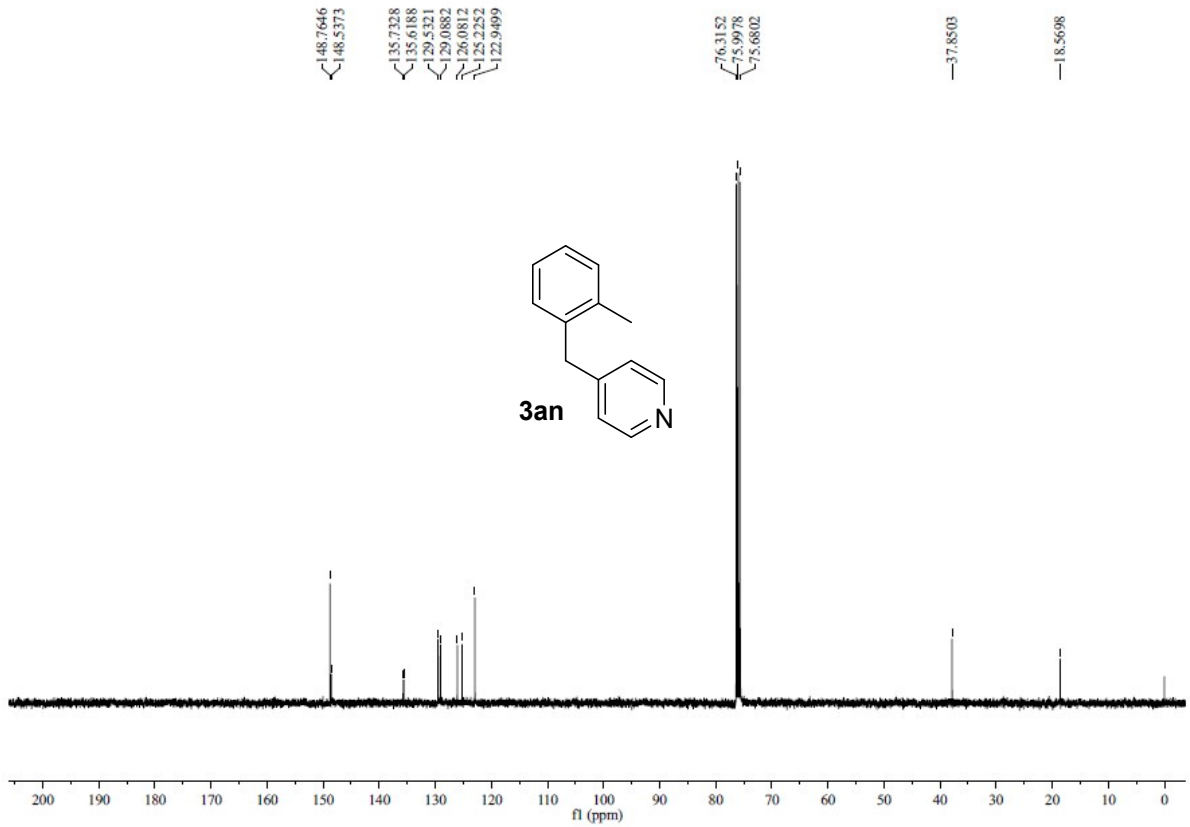
8.4074
8.3999
8.3961
7.1897
7.1328
7.1237
7.1189
7.1098
7.1007
7.0969
7.0867
7.0443
7.0343
7.0318
7.0242
6.9702
6.9553
3.9071
2.1331
3an
N
f1 (ppm)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135.6188
129.5321
129.0882
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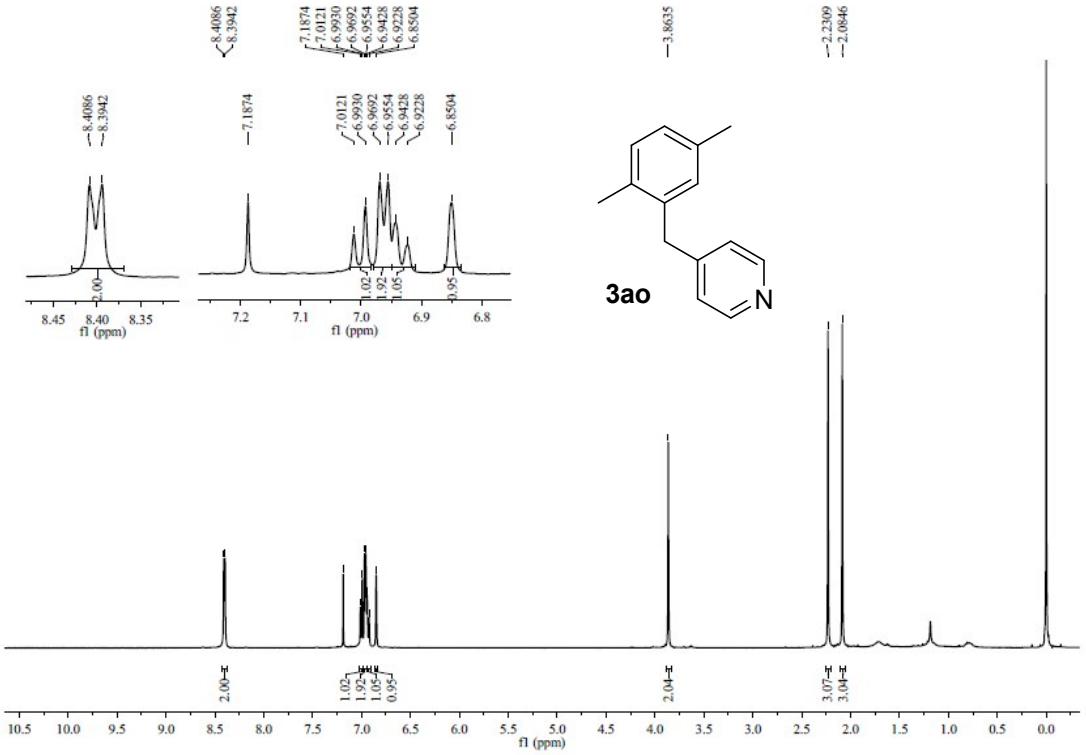
75.6802
37.8503
18.5698
3an
N
f1 (ppm)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7.1874
7.0121
6.9930
6.9692
6.9554
6.9428
6.9228
6.8504
3.8635
2.2309
2.0846
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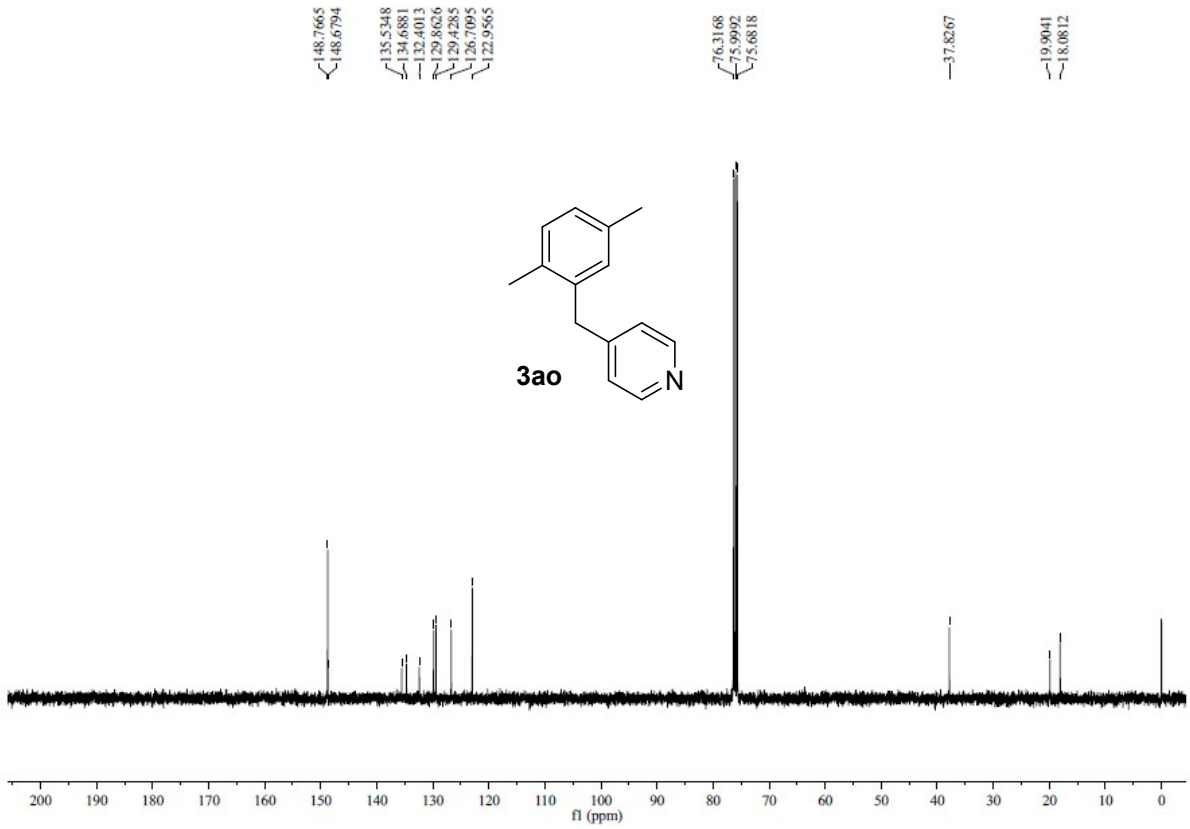
f1 (ppm)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148.6794
135.5348
134.6881
132.4013
129.8626
129.4285
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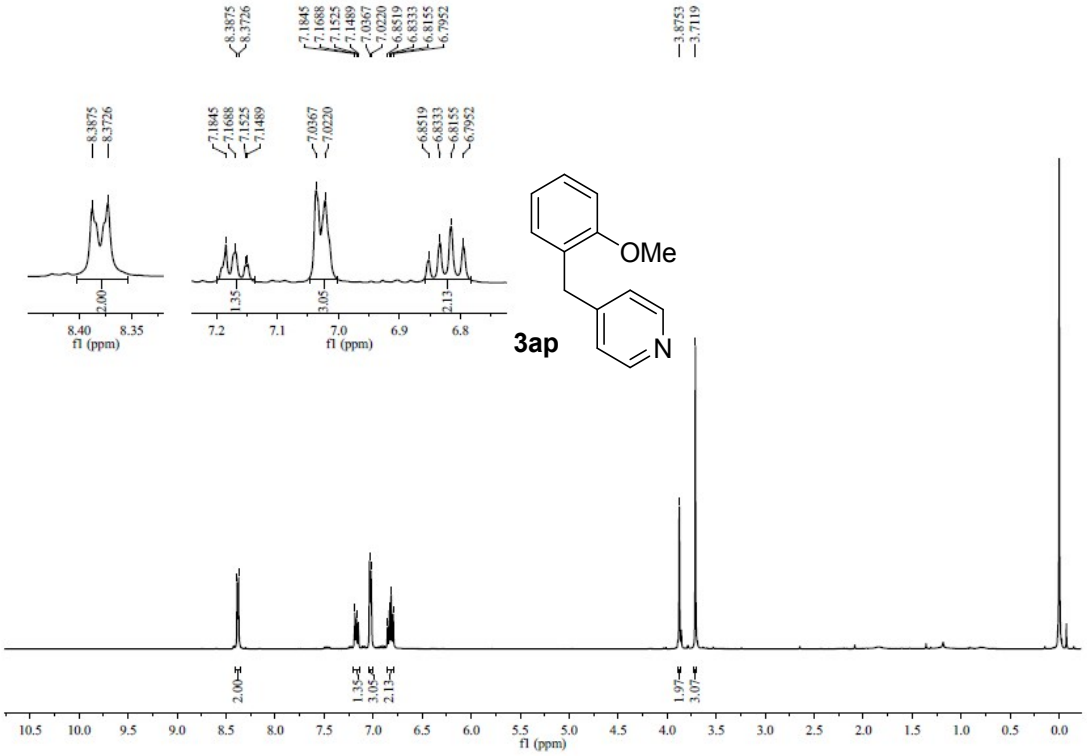
76.3168
75.9992
75.6818
37.8267
19.9041
18.0812
3ao
N
f1 (ppm)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7.1845
7.1688
7.1525
7.1489
7.0367
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6.8333
6.8155
6.7952
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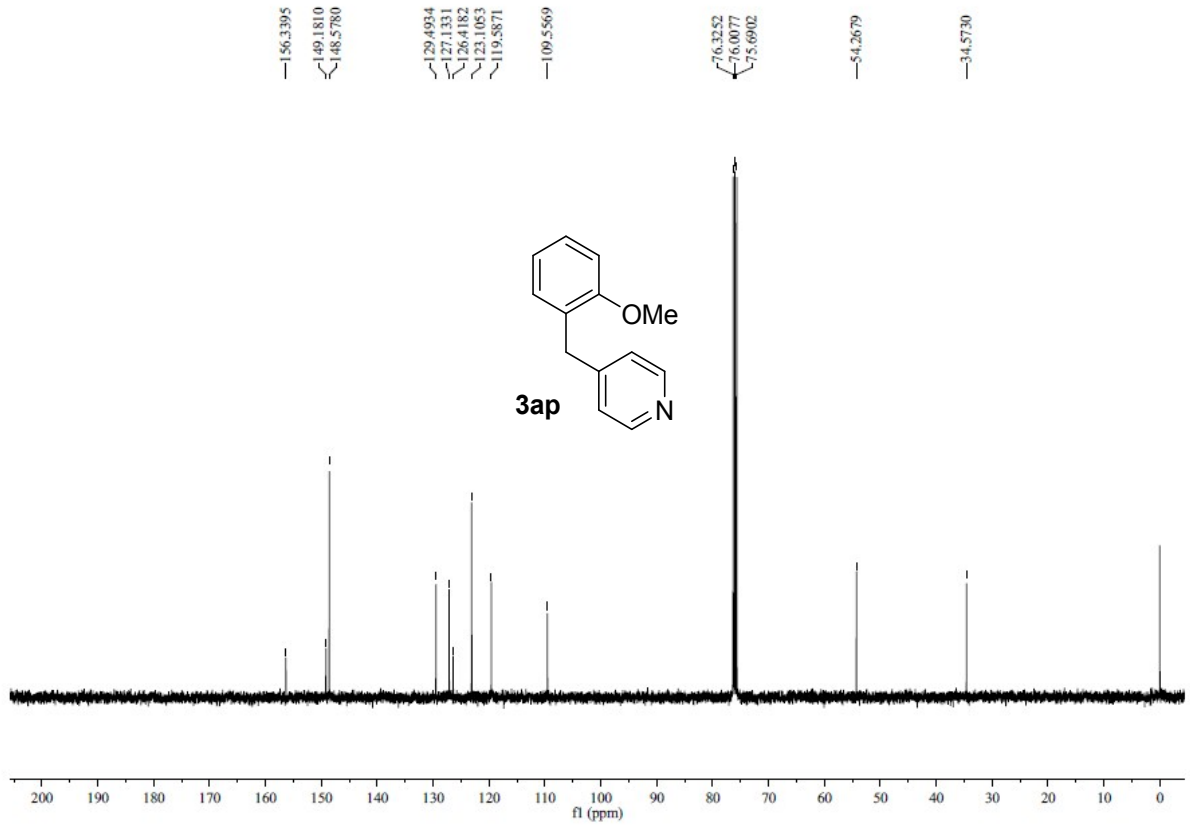
3.7119
OMe
N
3ap
fl (ppm)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129.4934
127.1331
126.4182
123.1053
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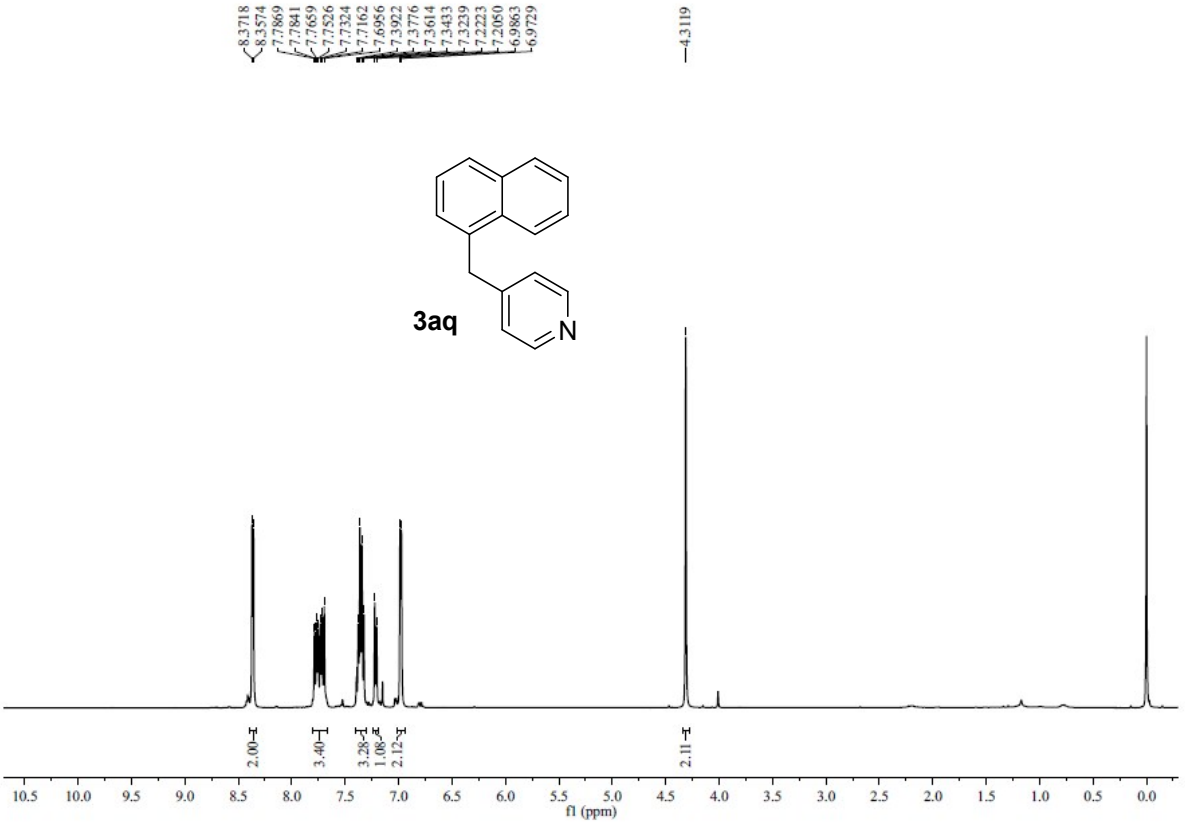
75.6902
54.2679
34.5730
OMe
N
3ap
fl (ppm)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7.7841
7.7659
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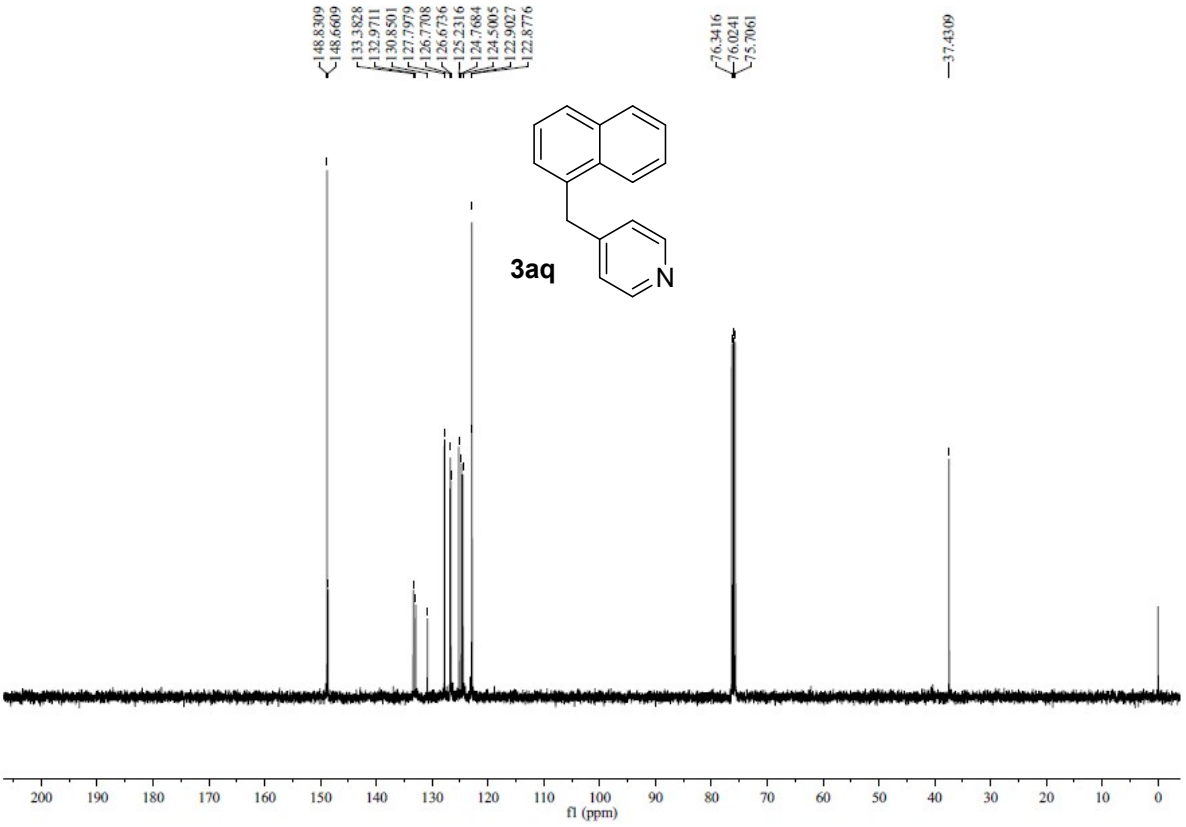
7.7324
7.7162
7.6956
7.3922
7.3776
7.3614
7.3433
7.3239
7.2223
7.2050
6.9863
6.9729
4.3119
3aq
N
2.00
3.40
3.28
1.08
2.12
2.11
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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122.9027
122.8776
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75.7061
37.4309
3aq
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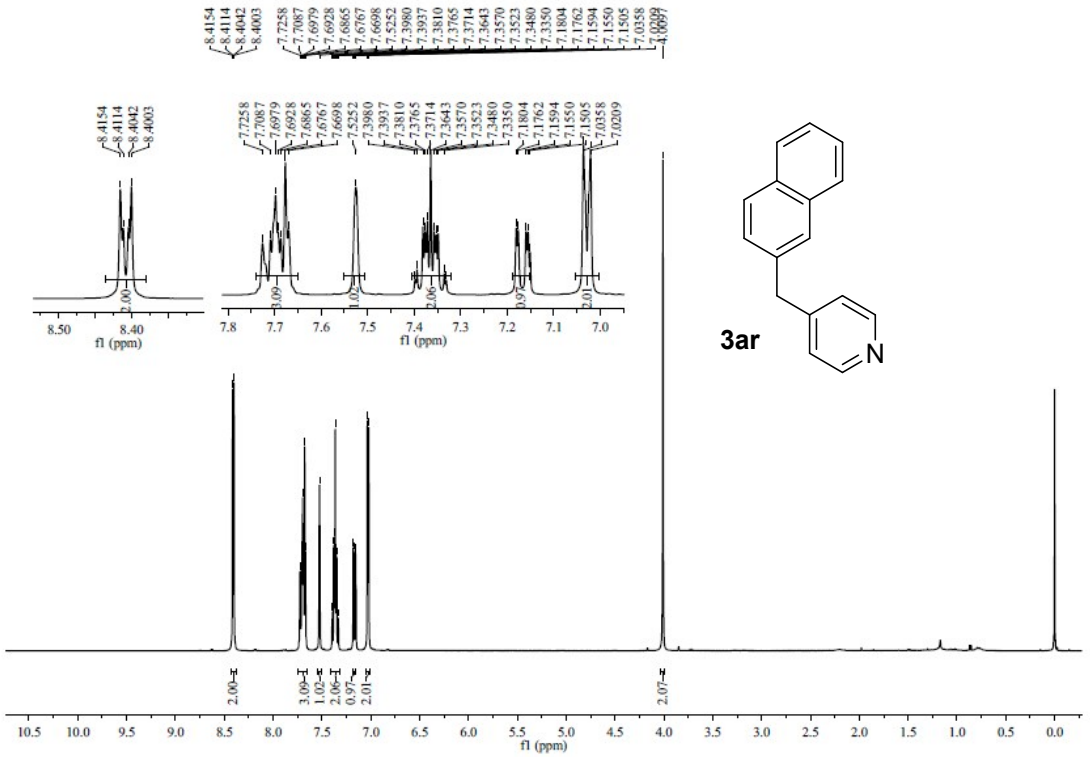
f1 (ppm)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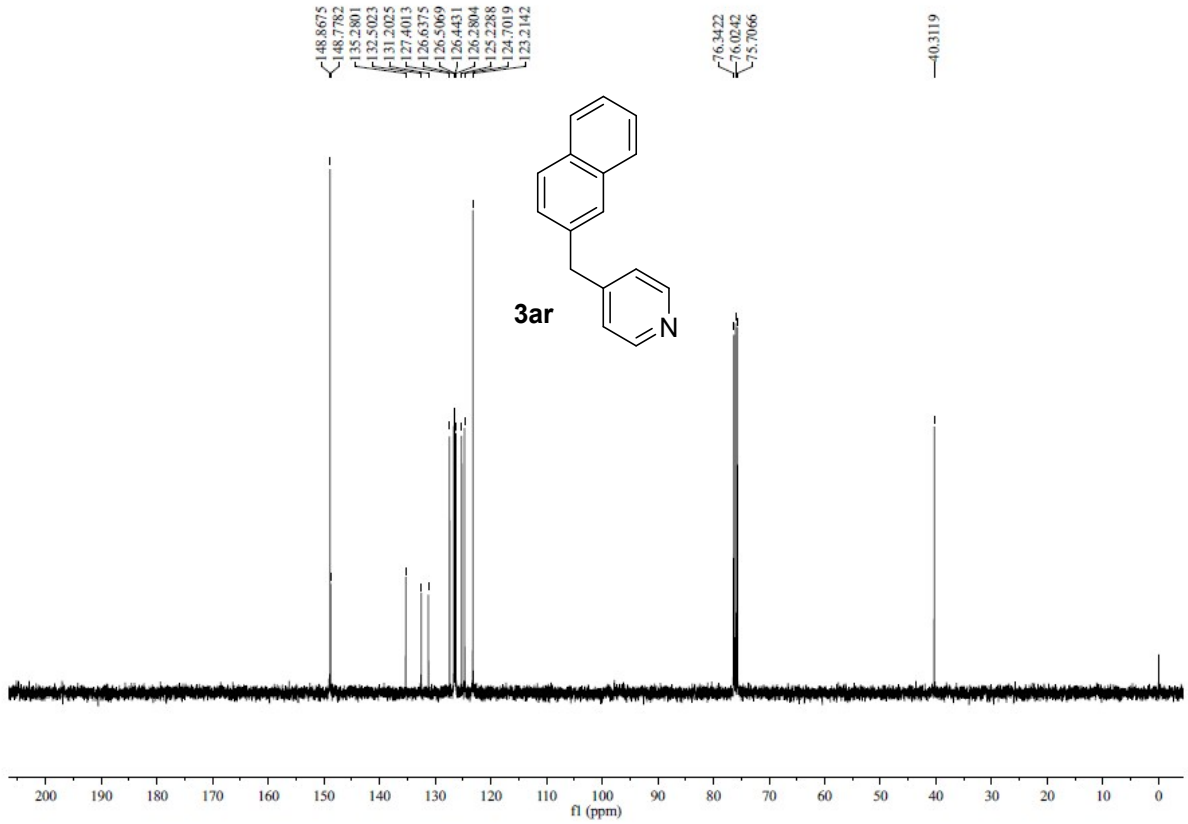
fl (ppm)


3ar
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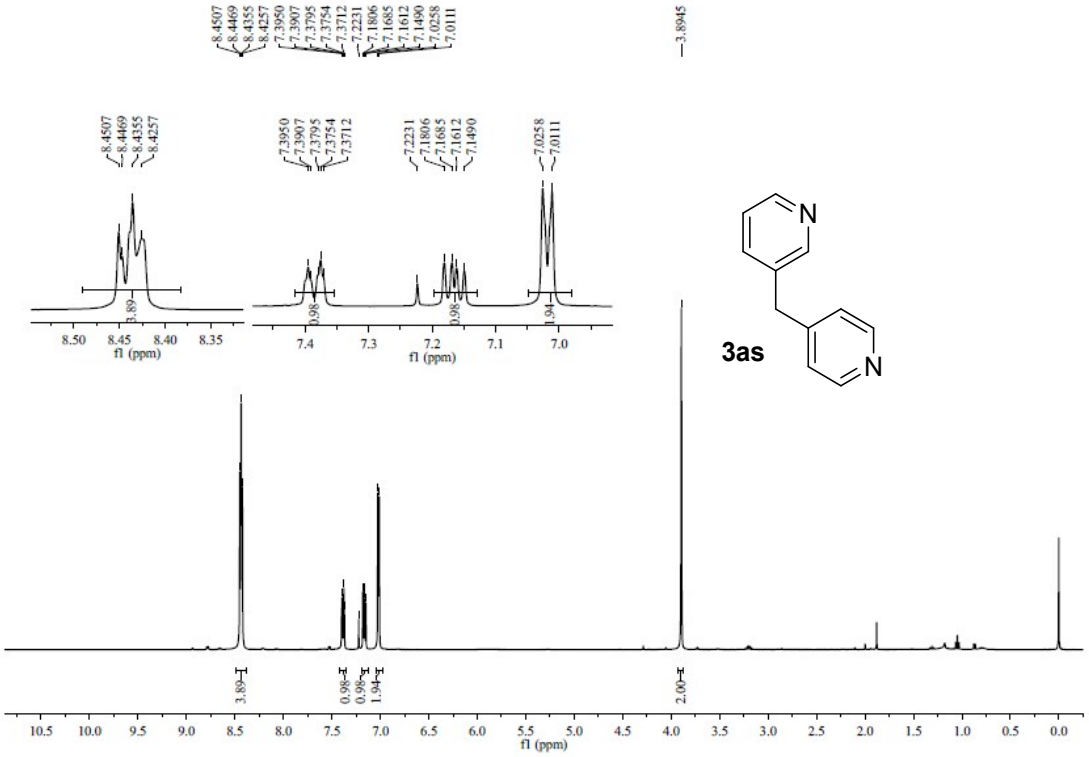
fl (ppm)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7.2231
7.1806
7.1685
7.1612
7.1490
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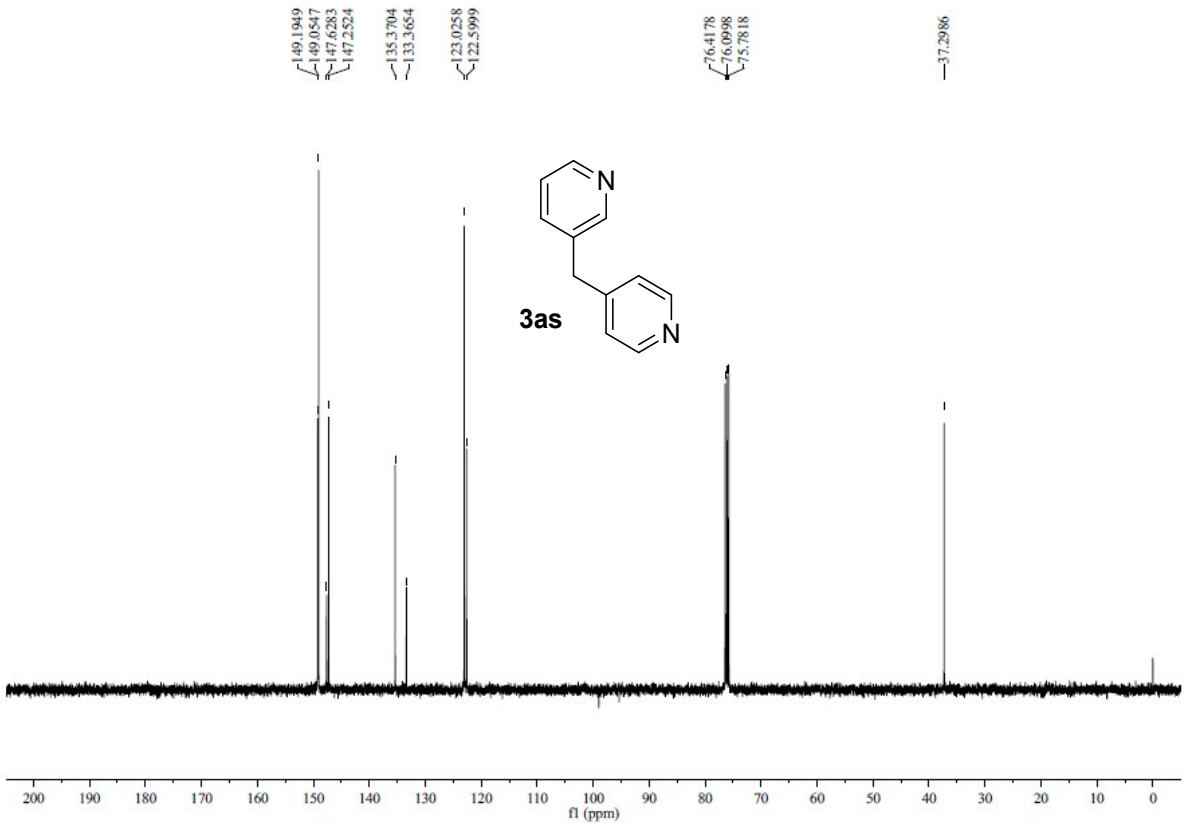
3.89
0.98
0.98
1.94
2.00
fl (ppm)
3as
N
N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3as
N
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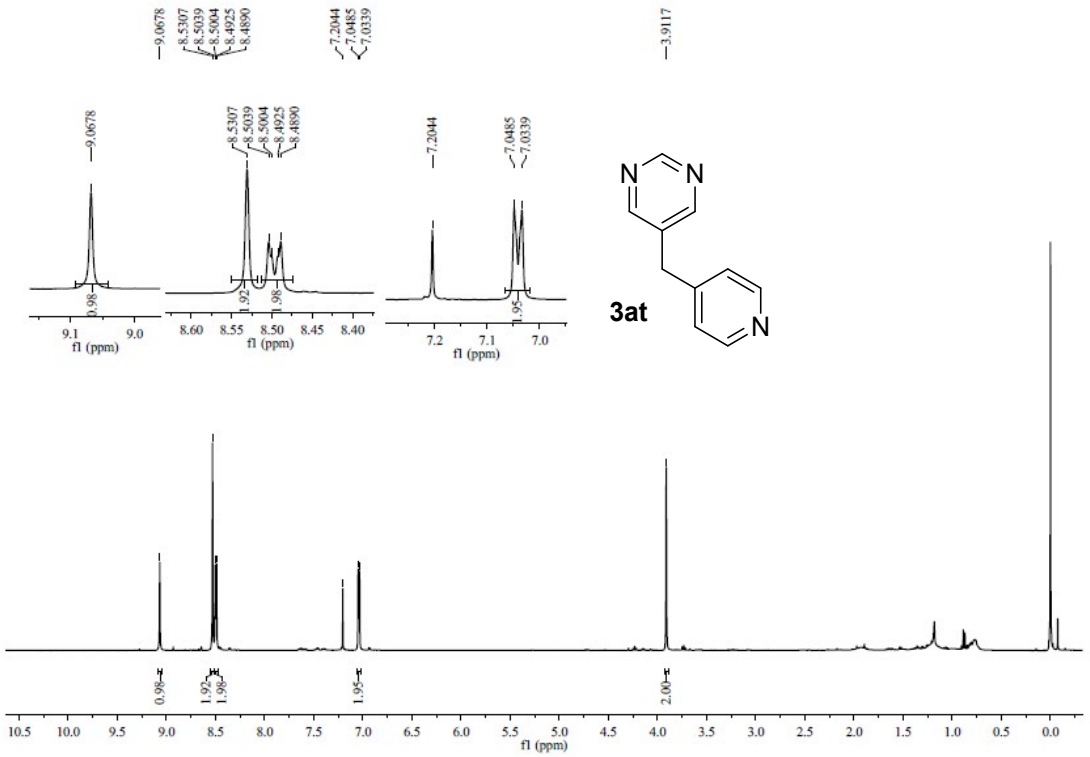
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7.0339
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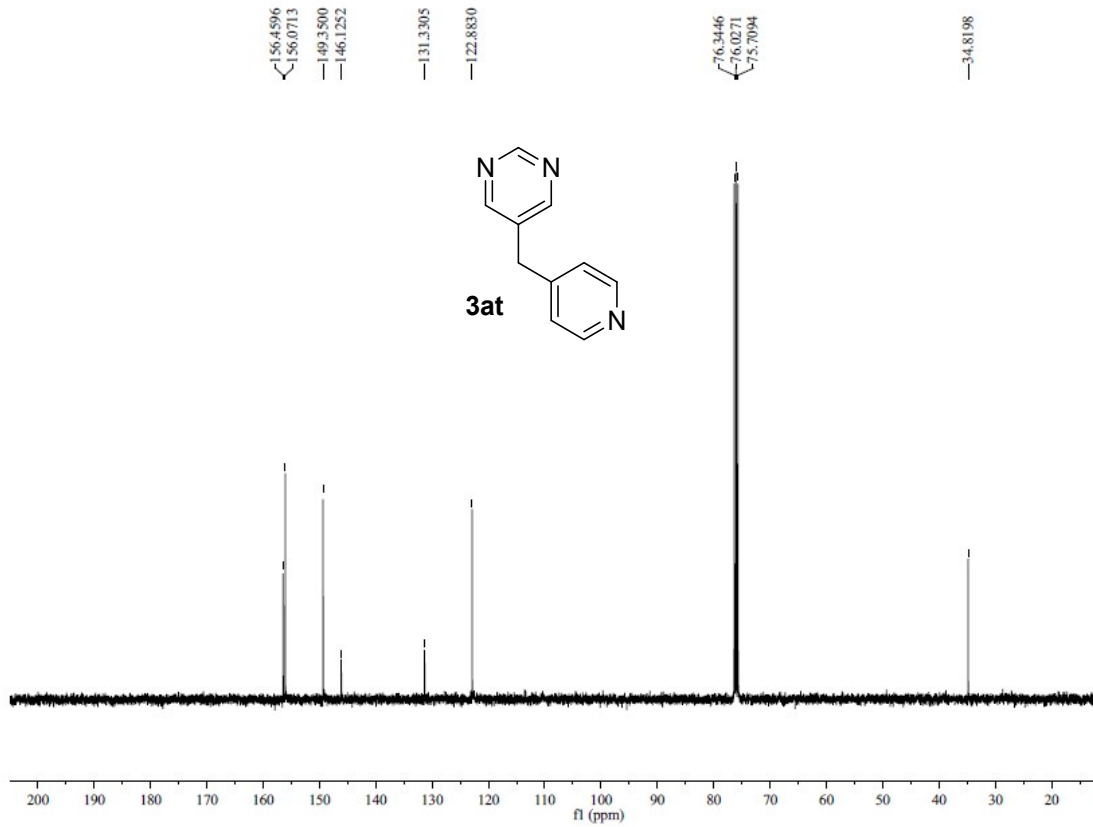
3at
f1 (ppm)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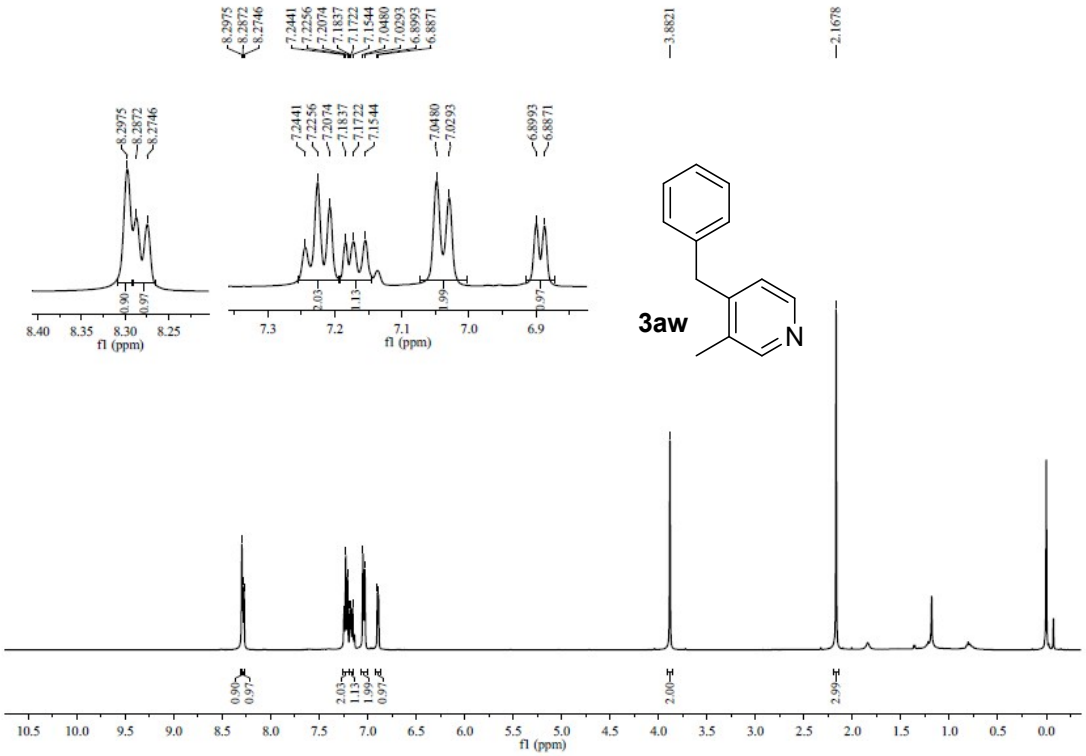
f1 (ppm)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3.8821
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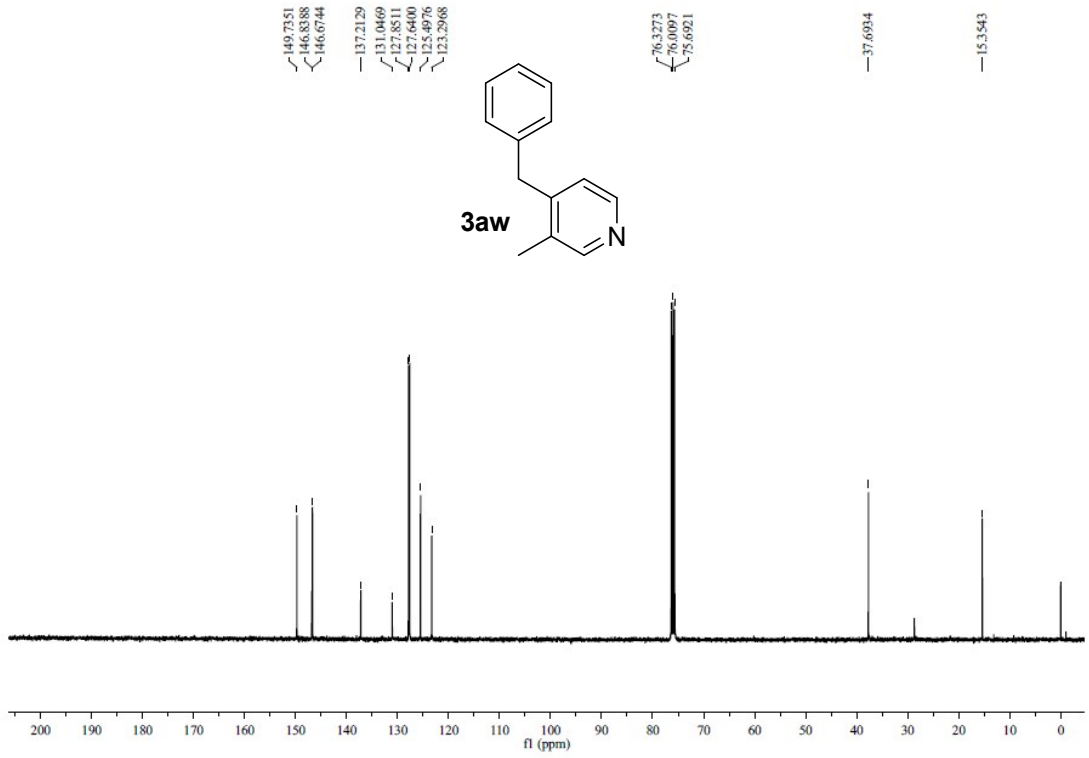
fl (ppm)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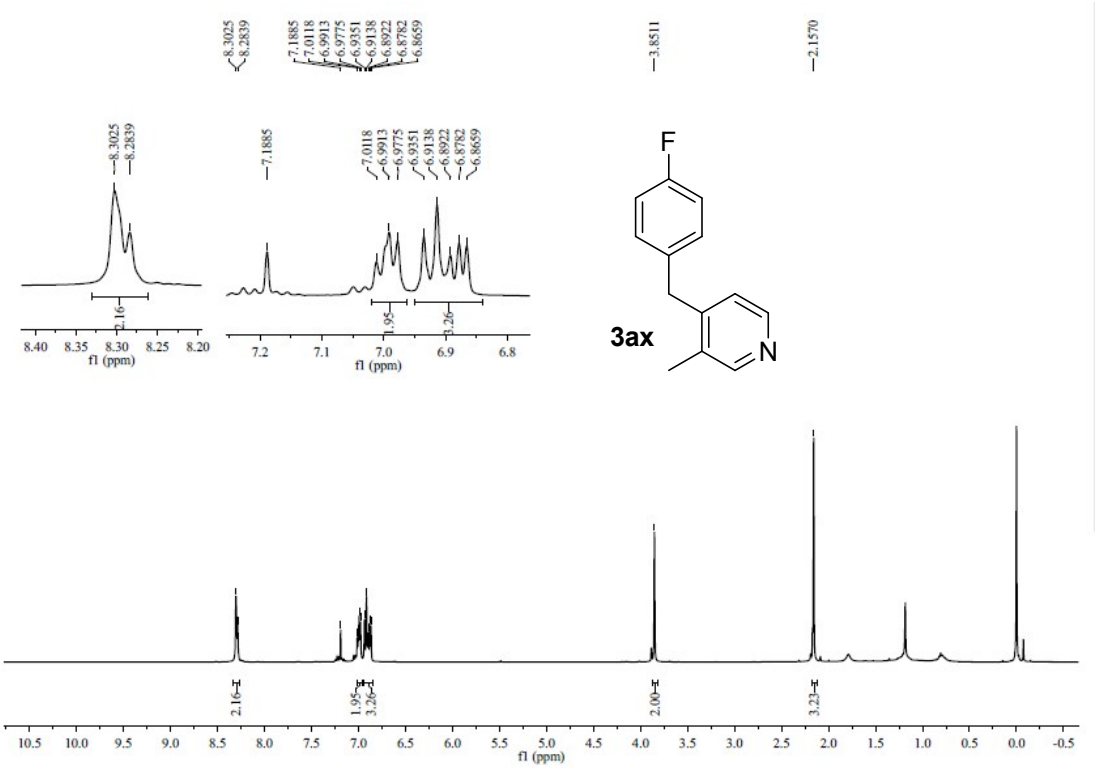
fl (ppm)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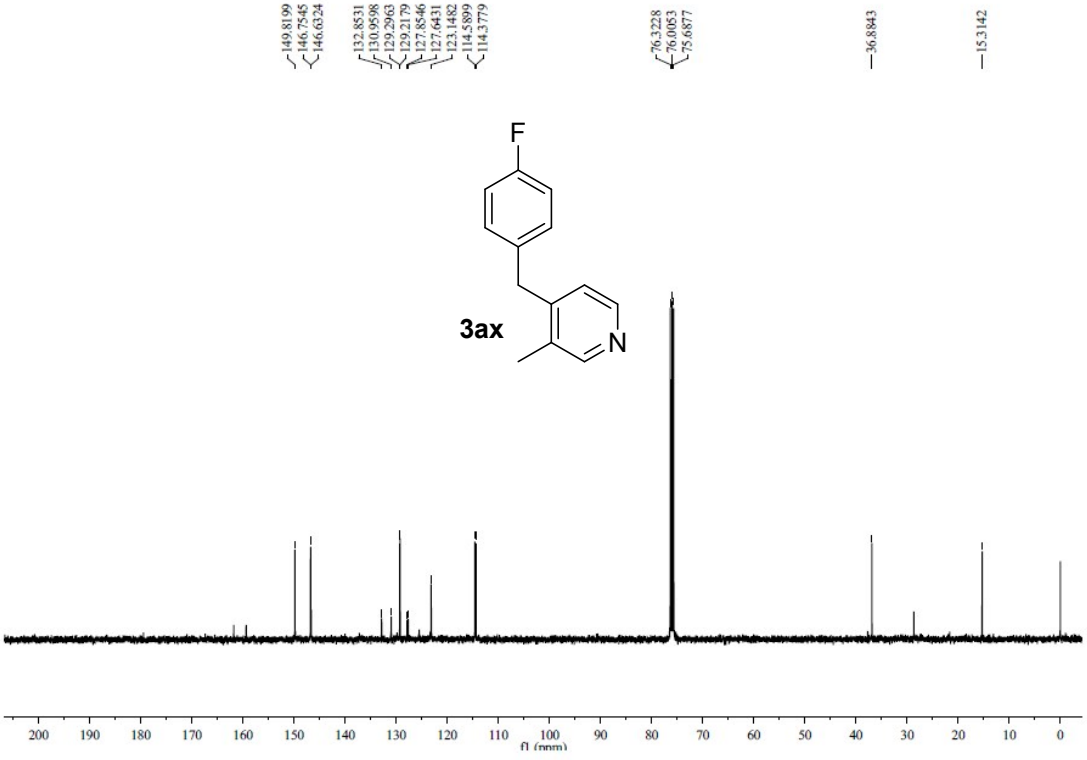
6.9138
6.8922
6.8782
6.8659
3.8511
2.1570
2.16
1.95
3.26
fl (ppm)
F
3ax
N
2.16
1.95
3.26
2.00
3.23
fl (ppm)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146.6324
132.8531
130.9598
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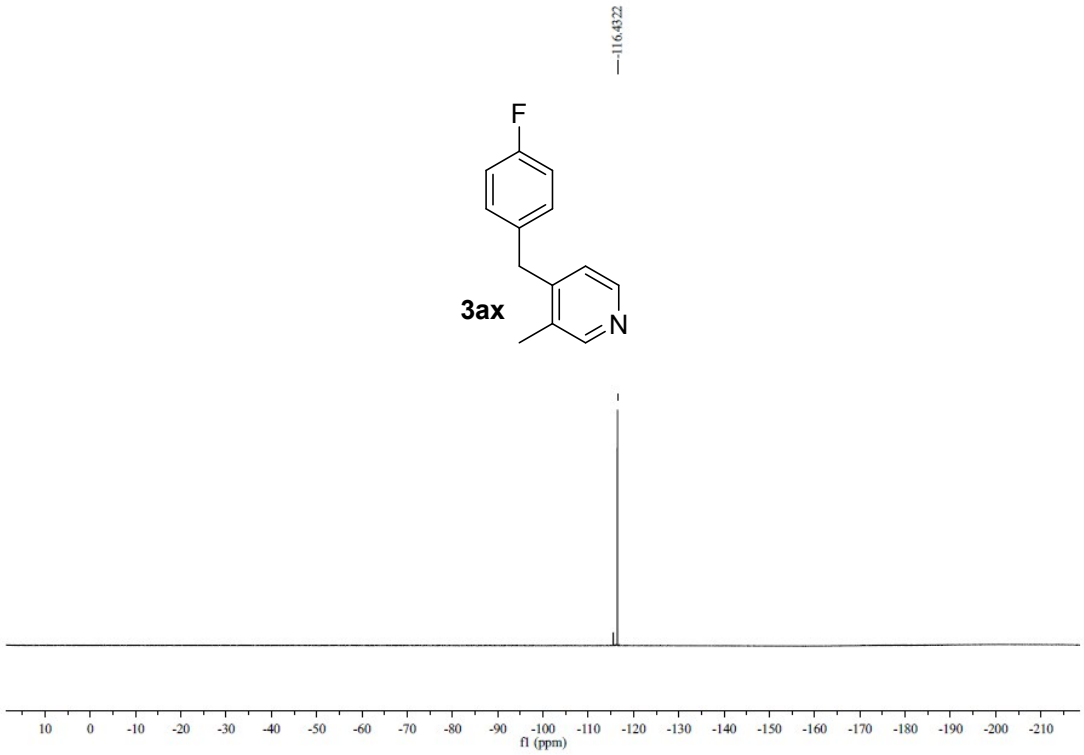
127.6431
123.1482
114.5899
114.3779
76.3228
76.0053
75.6877
36.8843
15.3142
F
3ax
N
fl (ppm)


-116.4322
F
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N
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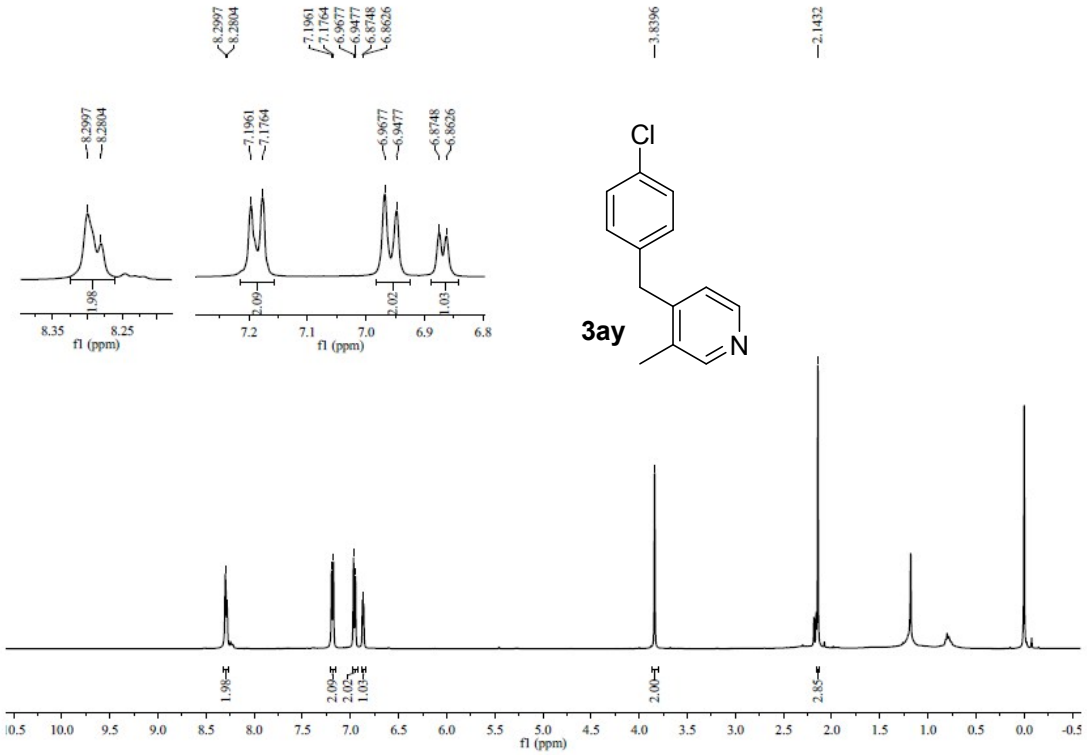
f1 (ppm)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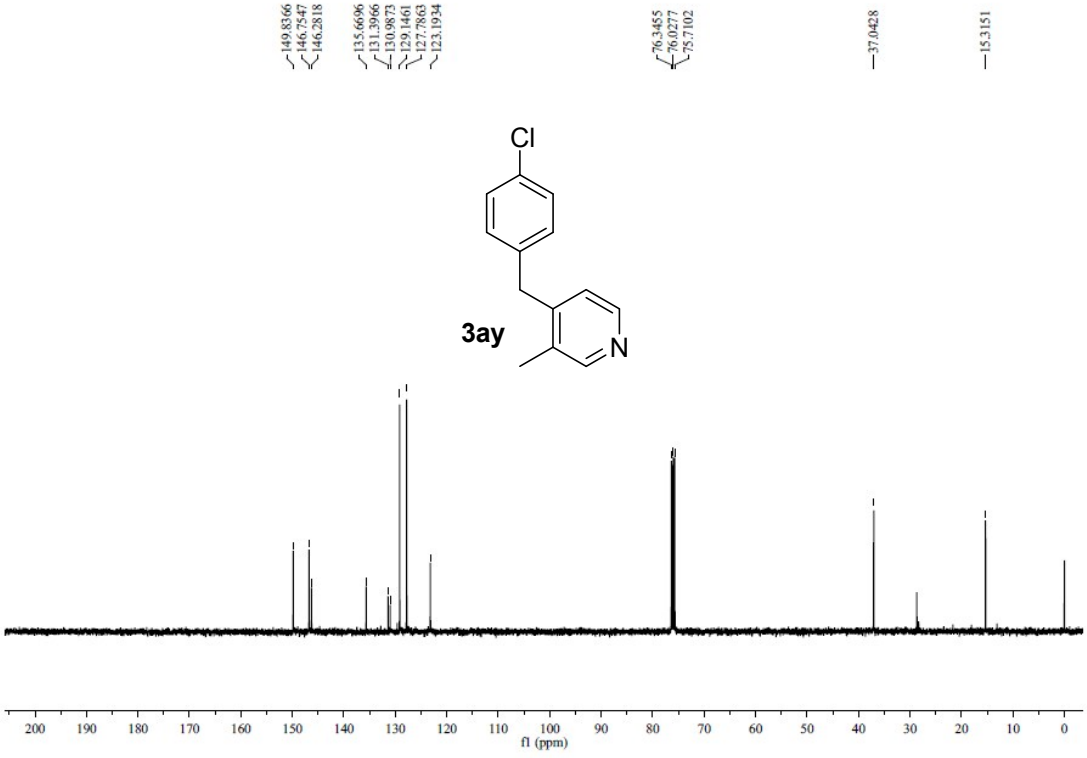
8.2804
7.1961
7.1764
6.9677
6.9477
6.8748
6.8626
3.8396
2.1432
Cl
3ay
N
1.98
2.09
2.02
1.03
2.00
2.85
fl (ppm)


149.8366
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146.2818
135.6696
131.3966
130.9873
129.1461
127.7863
123.1934
76.3455
76.0277
75.7102
37.0428
15.3151
Cl
3ay
N
fl (ppm)